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No. 23.—OCTOBER, 1904

DEPARTMENT OF THE INTERIOR  
BUREAU OF GOVERNMENT LABORATORIES  
BIOLOGICAL LABORATORY

# THE PLAGUE: BACTERIOLOGY, MORBID ANATOMY, AND HISTOPATHOLOGY

INCLUDING A CONSIDERATION OF INSECTS  
AS PLAGUE CARRIERS



BY

MAXIMILIAN HERZOG, M. D.

MANILA  
BUREAU OF PUBLIC PRINTING  
1904

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## LETTERS OF TRANSMITTAL.

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DEPARTMENT OF THE INTERIOR,  
BUREAU OF GOVERNMENT LABORATORIES,  
OFFICE OF THE SUPERINTENDENT OF LABORATORIES,  
*Manila, October 20, 1904.*

SIR: I have the honor to transmit herewith an article entitled "The Plague: Bacteriology, Morbid Anatomy, and Histopathology (including a consideration of insects as plague carriers)." by Maximilian Herzog, M. D.

I am, very respectfully,

PAUL C. FREER,  
*Superintendent Government Laboratories.*

Hon. DEAN C. WORCESTER,  
*Secretary of the Interior, Manila, P. I.*

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DEPARTMENT OF THE INTERIOR,  
BUREAU OF GOVERNMENT LABORATORIES,  
BIOLOGICAL LABORATORY, OFFICE OF DIRECTOR,  
*Manila, October 19, 1904.*

SIR: I have the honor to transmit herewith and to recommend for publication a report entitled "The Plague: Bacteriology, Morbid Anatomy, and Histopathology (including a consideration of insects as plague carriers)," by Dr. Maximilian Herzog, pathologist Biological Laboratory.

Very respectfully,

RICHARD P. STRONG,  
*Director Biological Laboratory.*

Dr. PAUL C. FREER,  
*Superintendent Government Laboratories.*



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# THE PLAGUE: BACTERIOLOGY, MORBID ANATOMY, AND HISTOPATHOLOGY.

(INCLUDING A CONSIDERATION OF INSECTS AS PLAGUE CARRIERS.)

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By MAXIMILIAN HERZOG, M. D., *Pathologist Biological Laboratory.*

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## PREFACE.

The "Great Black Death," the most dreaded scourge of the Middle Ages—the grim reaper who, as is estimated, in the fourteenth century, within three years, carried away in Europe twenty-five millions of people—had, as it seemed, vanished from the surface of the globe, when about ten years ago a new great pandemic of plague, which still persists, appeared in China and India. From here it made excursions into London, Oporto, Glasgow, Triest, Alexandria, Sidney, Hamburg, Bremen, and Naples—however (thanks to the modern methods of meeting infectious and contagious diseases), without there gaining a foothold or assuming dangerous epidemic proportions.

At present the dreaded disease has not merely reached our own Far Eastern, transoceanic possessions—the Philippine Islands—but it has even established itself endemically in California at San Francisco. While it is to be hoped that with proper vigilance and with a continuous, untiring practice of the prophylactic measures which we are taught by modern hygiene the plague may never assume dangerous epidemic proportions, either in the Philippines or in the United States, we have every reason to keep it in view and to study it carefully in all of its phases. Therefore we need not apologize for offering in this bulletin a contribution to the bacteriology, morbid anatomy, and histopathology of plague as gained from both a perusal of literature and more particularly from

a study of a number of cases which came to post-mortem examination in Manila.

It has been my purpose in the preparation of this report to furnish a scientific contribution to the subject and to bring out, if possible, some new points, which might be of interest and value. However, another practical object has never been lost sight of, namely, to provide a guide for those who might be called upon to make a post-mortem diagnosis of the first case of suspected plague in a district. This will always be a matter of great responsibility and sometimes one of considerable difficulty. Unless circumstances compel the contrary, the diagnosis of a plague case, being the first of its kind in a community, on board of a ship, etc., should be confirmed by one well trained in general pathology and bacteriology; or, still better, by one also having experience in the recognition and examination of plague cases.

The importance of promptly diagnosing the first case of plague can not be overestimated. This disease does not make its initial appearance as a widespread epidemic, as is often the case with Asiatic cholera, when caused by a contaminated water supply or from other sources of infection. Rather, it begins very insidiously from one or several imported cases. It is frequently easy to hold the plague in check, provided it is recognized and properly fought at an early stage. This has been proved by the observations made in the cities mentioned above and in Manila.

In studying the histopathology of plague a highly interesting change was found in the kidneys, namely, extensive and frequently occurring hyaline fibrin thrombosis of the glomerular capillaries. As it appears that this change has not been described in the study of the microscopic anatomy of the disease, it has been considered somewhat at length. The histologic examinations in their entirety have led to the conviction that plague in its most common bubonic type should not be looked upon as a hemorrhagic septicæmia, because according to all appearances the infecting bacilli remain practically localized until the agonal stage of the disease is reached.

One of the cases examined and herein reported in detail suggested the possibility, if not the probability, of an infection through the agency of pediculi. This led to the study of the rôle which insects may play as carriers of plague. The ones which have been accused particularly of being the most important factors in

spreading plague from rats to men are the rat fleas. In taking up this question with reference to local conditions, it was found that these rodents in Manila are infested by a species of *siphonaptera* not heretofore described. It, however, appears that this new species of flea has not taken any part in the conveyance of the disease, which may or may not have been first imported to this city through the agency of rats.

It is a source of great satisfaction to the writer to be in a position to present this paper well illustrated with colored plates, photographs, and microphotographs, by which whatever value it possesses, both as a scientific contribution and as a guide in the post-mortem diagnosis of plague, is undoubtedly greatly enhanced.

For a revision of the manuscript the author is indebted to Drs. Paul C. Freer and Richard P. Strong. The colored drawings were prepared by Mr. T. Espinosa and Mr. W. Schultze and most of the microphotographs by Mr. Chas. Martin, all members of our laboratory staff.

#### THE DISCOVERY OF THE PLAGUE BACILLUS.

The etiologic factor of plague in all of its various forms is a specific micro-organism—the plague bacillus. It can generally, without difficulty, be cultivated in pure culture from cases of plague in man. In susceptible animals it produces a disease identical with or similar to that found in the human race, and in some deplorable laboratory accidents, in locations where no plague existed, it has caused typical fatal pest infection in men. The names both of Yersin and of Kitasato are connected with the discovery of the plague bacillus during the epidemic in Hongkong in 1894. To the claims of each of these investigators to be the independent discoverer of the plague germ one may well apply the words of the German poet, that it is “Von den Parteien Hass und Gunst entsteht.”

Some writers upon plague dispute Yersin's claim; while not a few, and particularly his own countrymen, maintain that Kitasato is not entitled to any fame in connection with the original finding of *Bacillus pestis*. Ogata, for instance, tersely states:

Many authors believe that the plague bacillus of Kitasato and that of Yersin are identical, but such is not the case. They are two absolutely different kinds of bacilli.

And then Ogata as well as Yamagiwa, in another publication, shows that they found the Yersin bacillus as the cause of the plague in the Formosa epidemic. Scheube equally opposes Kitasato's claim and says:

The bacillus discovered simultaneously and at the same place by Kitasato is not the true plague bacillus (discovered by Yersin), because it shows marked points of difference, it is motile, etc.

It is a somewhat ludicrous misfortune which befalls Scheube in his polemical remarks against Kitasato, that he himself confuses some of the differentiating characters of Yersin's and Kitasato's first descriptions. Scheube makes it appear as if Kitasato at first erroneously stated that the plague bacillus does not and that Yersin's bacillus does retain Gram's stain. The opposite, of course, is true. Yersin correctly, in his first report, stated that the plague bacillus loses Gram's stain.

On the other hand, Cantlie, of the Indian Medical Service, at a plague conference and discussion held in London in 1898 observed that the names of Kitasato and Yersin were usually associated, and the bacillus was commonly termed the Kitasato-Yersin bacillus. Kitasato, however, had demonstrated the bacillus a week previous to Yersin, and although he (Cantlie) felt the greatest respect for the work of Yersin on plague, yet the latter had no claim as an independent discoverer of the bacillus, since that distinction belonged to Kitasato alone. (*Brit. Med. Jour.*, 1898, Vol. II, Sept. 24, p. 962.)

However, anyone who reads the reports of Yamagiwa and Ogata regarding the epidemic in Formosa, which contain literal translations from Kitasato's first publications in Japanese, can not fail to conclude that it was indeed Yersin and not Kitasato who had first worked with pure cultures of the plague bacillus. Kitasato's first reports show clearly that what he described as pure cultures of the plague bacillus were not such. On the other hand, there can be no reasonable doubt that Kitasato saw and recognized plague bacilli shortly before Yersin. No bacteriologist examining the juice of buboes in certain stages, either from the living or from the post-mortem table, can overlook the enormous number of characteristic bacilli. However, it was undoubtedly Yersin who first isolated and described what was really a pure culture of the plague bacillus.

Yersin's first published description was submitted to the French Academy and reads as follows:

The first bacteriologic researches were made on living subjects. An examination of the blood drawn from the finger at various periods of the disease failed to show the microbes, and the inoculations remained sterile. The buboes, on the contrary, contained an abundance of a pure culture of a very small, short bacillus, with rounded ends, which does not stain by Gram's method, but does with Gentician violet. I have found this bacillus in buboes of eight patients, and in two plague autopsies I have found the same microbe. It is particularly numerous in the buboes, less abundant in the other (lymphatic) ganglions, and very rare in the blood at the moment of death. The liver and spleen are increased in size and contain the specific bacillus.

A short account of some animal experiments with post-mortem findings forms the conclusion of Yersin's first report. The second one gives an equally correct—in some respects more elaborate—description of the bacillus, of its cultivation, and of animal experiments. Kitasato, in his first description in the *London Lancet* (August 25, 1894), states that the bacilli are to be found in the blood, in the buboes, in the spleen, and in all the internal organs of the victims of the disease.

I am at present [he says] unable to say whether or not Gram's double-staining method can be employed. The bacilli show very little movement.

Metschnikoff's standpoint in the controversy as to the discovery of the plague bacillus is perhaps the most correct and the most impartial one, hence we quote his words in the language of the original. He says:

Yersin apres des recherches laborieuses effectuées dans des conditions particulièrement difficiles, decouvrit le microbe pesteux. Independamment de lui Kitasato arrivait au meme resultat. Le savant japonais s'est borné a communiquer quelques notes preliminaires sur ce sujet, tandis que Yersin en a poursuivi l'etude avec persévérance; c'est donc a lui que nous devons le meilleur de nos connaissances actuelles sur la peste.

#### MORPHOLOGY OF THE PLAGUE BACILLUS.

The bacillus *pestis* is quite variable in its morphology, and it is important to remember this fact in connection with the bacteriologic diagnosis of the disease. In post-mortem smears prepared from a recent nonsuppurating primary bubo, from a pneumonic focus, from the spleen, and occasionally from other internal organs one generally finds numerous plague bacilli. In those from the

primary bubo and from the pneumonic foci their number is legion. In smears from the spleen they are fairly abundant, while in preparations from the other organs, according to our own experience, they are generally present only to a moderate extent, unless septico-pyemic metastatic foci should have been established, when they may be quite numerous. In smears prepared from the heart's blood we have always found very few bacilli, even in pneumonic and septico-pyemic cases.

As a routine method for the examination of smears we have adopted the following procedure: The preparations were made during the post-mortem examinations on slides, and these, as soon as air-dry, were placed in a wide-mouthed bottle containing absolute alcohol. Here they remained until after the termination of the autopsy, when they were stained with dilute carbol-fuchsin (1 part of the original stain to 5 to 10 aqua destillata) for twenty to forty seconds, and then freely washed with water. They were next immediately examined with oil-immersion magnification. If it was found that the stain was not satisfactory, being either too light or too heavy, the immersion oil was washed off in xylol and the shortcomings corrected either by a second prolonged dyeing or by rapid immersion in alcohol, followed by washing in water. However, after a little practice it is soon possible correctly to estimate the time necessary to bring about that particular stain which will best show the characteristic morphologic features of the bacillus, and a second attempt is rarely necessary. If after the first examination of the slides it is desirable to preserve them for future reference, the immersion oil is washed off in xylol and the specimens may now be mounted permanently in Canada balsam, being protected by a cover slip.

In smears made from the organs the plague organism appears as a rather short, plump bacillus, being 1.5 to 1.75  $\mu$  long and 0.5 to 0.75  $\mu$  thick; generally the proportion of width to length is as one to two. Individuals considerably longer than 1.75  $\mu$  are occasionally seen. The bacilli are generally single, occasionally diplobacilli are encountered, and very rarely short chains. In smears which have been fixed in absolute alcohol and which have been properly dyed the bacilli are not uniformly colored, but they show a distinct polar staining. Frequently the whole periphery of the bacillus is stained and only the center has remained uncolored. Other forms of the organism, while differing in certain respects

from the above-given description and while not representing the most characteristic type, are so frequently found in smears that the student of plague must thoroughly familiarize himself with them. These are elliptical or egg-shaped, or almost spherical, and they show only a very narrow peripheral staining, or they may not stain at all; hence they look like mere empty shells, which indeed they probably are, since they are most commonly found in older buboes. Also, in smears from cases which have succumbed only after several days' sickness, one frequently sees various involution forms of the plague micro-organism, which appear like yeast cells or which are either quite hazy and indistinct or club shaped and irregular in outline. Sata has shown that such involution forms may be seen on and after the fourth day in experimental plague infection in animals. In cover-glass preparations from pure cultures the bacilli are not so characteristic as we find them in smears from human plague cases, except in some involution forms to be more fully described below. The first generation, as a rule, shows the polar staining and the unstained center fairly well, but in subsequent ones these features often become more or less indistinct, or may even entirely be lost. Plague bacilli from pure cultures, particularly from the water of condensation of agar tubes, or from bouillon, frequently show shorter or longer chains, in which dividing lines between the individual bacilli are so indistinct as to cause them to appear like filaments. Involution forms are likewise liable to present themselves early even on favorable media. We have occasionally seen them as soon as the second or third day on agar tubes.

The plague bacillus may be stained with any one of the watery solutions of the common basic aniline dyes. The carbol-thionin stain, frequently mentioned in connection with it, is not to be recommended if one works in the Tropics, since for certain reasons it is very liable to fade. Kossel's modification of Romanowsky's stain has not been very satisfactory in our hands, and for general practical purposes we have found dilute carbol-fuchsin used in the manner above recommended the most simple and most uniformly reliable.

The plague bacillus, if treated by Gram's method, is decolorized.

The bacillus, if grown in the animal body, possesses a capsule, which, however, is not very easy to demonstrate unless thin spreads are prepared and fixed in alcohol with great care. There is nothing

characteristic in the capsule, so its exhibition will not assist in the microscopic diagnosis of plague. The bacillus is not motile, does not possess any flagellæ, nor has spore formation been observed. Even if one occasionally sees in the bacilli bodies somewhat like spores, they are not genuine spores, because such bacilli are not more resistant to heat, antiseptics, etc., than the other pest bacilli.

#### CULTIVATION OF THE BACILLUS.

The plague bacillus grows on all ordinary laboratory culture media, best on such as are faintly alkaline. Even a minor degree of acidity as well as a higher degree of alkalinity prevents its development. It develops at temperatures ranging from 5° to 38° C., and in our artificial media best at 25° to 30° C. It is quite strictly, though perhaps not absolutely, obligate aërobic. As a rule it develops on artificial media only in the presence of free oxygen. However, some observers have occasionally seen a weak growth even in the absence of the latter. When a favorable solid culture medium (agar or gelatin, slightly alkaline) is inoculated from the organs (bubo, spleen, etc.) of a plague case, the development of the plague bacilli is at first generally quite slow, and frequently very little can be seen with the naked eye within the first twenty-four hours. On the other hand, in a considerable number of cases a typical picture may appear after this time and it is always present after forty-eight hours. The surface of the agar or gelatin shows small, delicate, round, moist, dewdrop-like colonies. They are light gray in reflected light and grayish-white in transmitted. If these colonies are inspected with a hand lens or with a lower power of the compound microscope they show an elevated, finely granular, rounded center and a perfectly transparent, very thin, flat marginal zone. The colonies on the whole are circular, but the transparent marginal zone early shows a somewhat irregular boundary line. Colonies of this type are not formed by any other micro-organism, except occasionally by the influenza bacillus. However, in the case of the plague bacillus they develop most characteristically on ordinary gelatin plates kept at 20° to 24° C., under which conditions the influenza bacillus would not show any growth at all. While these typical young colonies are seen both on agar and on gelatin, we think that they are best shown on the latter, hence the use of this medium is to be greatly recommended in the bacteriologic diagnosis of plague. Gelatin plates can, of course, be



used in the Tropics only where an incubator with cooling device is at hand. If an impression preparation is made of one of the young colonies with a homogeneous, transparent, marginal zone, it is seen that this consists of bacilli arranged in curved filaments. If the inoculation from the organs has been quite rich in plague bacilli the surface between the colonies has a ground-glass appearance, which becomes more marked after forty-eight hours, and is generally well seen in cultures a few days old. After three or more days the erstwhile very delicate colonies become larger, more granular, and less transparent. The marginal zone likewise has become thickened, is less homogeneous, and its edges become more irregular and are often finely serrated at the periphery. The colonies now have a more decidedly grayish-white appearance and occasionally show a slight tinge of yellow. In young cultures of the first generation colonies are usually small, grow slowly and remain comparatively small, occasionally, however, rapidly attaining a diameter of several millimeters. We have several times seen such large colonies where the material from which an inoculation was made contained few bacilli and where subsequently only a few colonies developed. However, this is probably not the only condition under which the large ones make their appearance. Older cultures of the plague bacillus, particularly when they have in consequence of evaporation become dry and quite granular, are somewhat iridescent. If a young plague culture is touched with a platinum loop it is found to be viscous and sticky. It is, however, easily removed from the surface on which it grows.

The plague bacillus, as stated before, early in its growth has a marked tendency to develop involution forms. As first shown by Hankin, this tendency is most pronounced in cultures on a 3 to 4 per cent salt agar. Hence we have in this medium one of the most valuable means for the bacteriologic diagnosis of plague. It is prepared and standardized like any ordinary agar, only that it does not merely contain one-half but 3 to 4 per cent of common salt. Hence, in case of an emergency, salt agar can be prepared from the ordinary media by the addition of the proper amount of NaCl to bring it up to the desired concentration. We have found it best to use a 3.5 to 4 per cent salt agar and not to diminish this percentage. On a medium of this concentration, particularly if it is fairly dry and contains very little water of condensation, involu-



tion forms of the plague bacillus are seen after twenty-four hours. Generally the greater number, or all, of the organisms from such a growth present themselves as large spherical bodies, looking very much like yeast cells; later, large swollen club or dumbbell shaped, spermatozoa-like or irregular forms make their appearance. The most typical, and the most constant form on a 3.5 to 4 per cent salt agar, after twenty-four to forty-eight hours, is the yeast-like, large, spherical plague organism. There is no micro-organism which forms this type so promptly and so regularly on salt agar and which might be confounded with the plague bacillus. Hence it is advisable in a first suspected plague case at the autopsy to inoculate besides gelatin plates also ordinary agar tubes, bouillon flasks, and salt agar tubes or plates. In bouillon flasks the bacilli, at temperatures between 30° and 35° C., after twenty-four hours, show a finely flocculent whitish, slowly increasing sediment. During the next twenty-four hours the flocculi extend upwards from the bottom along the walls. A fine whitish ring of growth then forms on the surface and in course of time covers it. If the flask is protected from any motion and kept perfectly undisturbed, bands and strands of bacilli finally grow downward from the surface membrane. The contents of the flask now present an appearance which somewhat reminds one of stalactite and stalagmite formation. A slight jar sends the stalactites to the bottom and destroys the characteristic appearance. The stalactite formation can be assisted by floating on the surface of the bouillon a few drops of an indifferent substance, such as butter, olive or cocoanut oil, small pieces of cork, splinters of wood, etc. Of course, these bodies should be added to the bouillon before sterilization. The bouillon used in connection with our plague work has been one of a fixed degree of alkalinity recommended particularly by Kossel and Overbeck as most favorable for the development of the plague bacillus. Such a bouillon is prepared in the ordinary manner and alkali is added until the broth is neutral to litmus, then 0.5 gram of crystallized soda is added to each 1,000 cubic centimeters. In bouillon cultures the plague organism has a marked tendency to form longer chains, which are composed of ten to twelve or even more small, short bacilli. Such chains on first sight appear much like streptococci, but a more careful examination reveals their proper structure. The individual links of the chain are not arranged in a perfectly straight line, but angles and bends are frequently seen.

The following facts may be added to the enumeration of the cultural peculiarities of the plague bacillus: It does not liquefy gelatin or blood serum, does not ferment dextrose, levulose, lactose, or mannit, grows sparingly on potato and on milk, which latter it does not coagulate.

In the preceding description of the morphology and of the cultural properties of the plague bacillus no attempt has been made to bring out all the details which have been reported in an extensive literature, but merely to state clearly and emphasize those points the knowledge of which is indispensable in the bacteriologic diagnosis of plague. Staining of the plague bacilli in sections will be referred to later.

### NOSOLOGY AND CLASSIFICATION.

Bubonic plague of man is an acute, occasionally more subacute, infectious disease, caused by a specific micro-organism, *Bacillus pestis*, which generally first gains entrance through a trauma of the skin or the mucous membranes and thence finds its way into some of the peripheral lymph glands. In other cases it is inhaled into the lungs, or in still others it enters directly into the general blood circulation. These different methods of infection at once suggest a classification into three main types—bubonic plague proper, plague pneumonia, and plague septicæmia. Perhaps the most prominent and most constant—certainly, even on superficial examination, the most manifest—pathologic feature of all forms of plague is the occurrence of hemorrhages both local at the site or sites where the plague bacilli are colonized in great numbers, as in the lymph glands and in the lungs, and general, subserous, submucous, parenchymatous, and interstitial hemorrhages. The great frequency and constancy of these hemorrhages in plague has led to its classification as a hemorrhagic septicæmia. Nothing, as we expect to be able to demonstrate, could be more false than such a definition of plague in man. It may be quite true that experimental plague in certain of the lower animals is indeed generally a hemorrhagic septicæmia, but this, of course, *a priori* proves nothing as to man. Anthrax, in some animals, is undoubtedly a septicæmia, yet usually when contracted by man it is primarily a local disease and frequently remains local. *Diplococcus pneumoniae*, when introduced experimentally into mice, rabbits, or

guinea pigs, produces a septicæmia, yet in man, under natural conditions of infection, it generally leads to a local infection of the lungs—lobar pneumonia. We have in another previous bulletin<sup>1</sup> called attention to the fact that all observations made on men show that the plague bacillus is not present at all early in the course of the disease in the general blood circulation. Our histologic examinations have further demonstrated that as a rule plague bacilli are either found not at all in the vascular system or are present in such very small numbers that an agonal or post-mortem invasion suggests itself.

It appears reasonable to limit the classification "septicæmia" to those infections in which a multiplication of the infecting micro-organisms obviously takes place in the general blood circulation. During the last few years a valuable diagnostic method of blood examination in acute infectious disease has been used quite extensively. Its results, however, have led to a misrepresentation of the character and classification of some diseases. This method is practiced as follows: From 1 to 5 cubic centimeters of blood, for instance, in a case of pneumonia or typhoid fever, are drawn from a vein and introduced into a culture flask containing from 50 to 200 cubic centimeters of nutrient broth. If now a pneumococcus or typhoid growth develops, it is concluded that there is in this case a general infection of the blood. But what does it really mean if 1 to 5 cubic centimeters of blood do contain a few bacilli which develop and multiply under the most favorable artificial conditions, conditions entirely different from those which prevail in the live, undiluted circulating blood? It certainly does not mean that these same micro-organisms could and would multiply in the circulating blood in the presence of antibodies and of many intact leucocytes. As it would be wrong to classify typhoid fever as a septicæmia, because typhoid bacilli enter the blood from the internal lymphatics, so it is wrong to classify ordinary bubonic plague as a septicæmia because some bacilli invade the blood from the infected lymphatics. If we do want to take cognizance of the frequency and of the extent of the hemorrhages in plague, we may define it as an infectious disease with general hemorrhagic toxæmia.

It was necessary early to enter into the discussion of this point

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<sup>1</sup> Herzog and Hare: Does Latent or Dormant Plague Exist Where the Disease is Endemic? Bulletin B. of G. L., Biological Laboratory, No. 20, I.

in order to explain and justify our opposition to the classification of plague in man as a general hemorrhagic septicæmia.

A study of the histopathology of plague suggests the following pathologic classification into a number of groups, viz:

- (1) Primary uncomplicated bubonic plague.
- (2) Primary bubonic plague with secondary septicopyemia.
- (3) Primary bubonic plague with secondary plague pneumonia.
- (4) Primary plague pneumonia.
- (5) Primary plague pneumonia with secondary septicopyemia.
- (6) Primary plague septicemia.

This classification does not, of course, include any secondary or tertiary complications due to micro-organisms other than the plague bacillus. We shall be able to illustrate all of these different types by cases investigated.

A number of writers have distinguished intestinal plague as a special form of the disease. Wilm, for instance, believes that the plague bacilli frequently enter the body of man through the gastro-intestinal tract and thus lead to a type which is well characterized both clinically and anatomically. Hossack says that 5 per cent of the plague cases occurring in the Calcutta epidemic of 1900 were of the intestinal type, and that 3 per cent of those in the one of 1896-97 were of a similar nature. Zupita reported a case of intestinal plague, but from its description it clearly appears that it was one of primary inguinal bubo, with primary buboes of the second and third order in the pelvic and abdominal cavities. In fact, we have failed to find in literature a single case which anatomically could be clearly classified as a case of intestinal plague. In our work special attention has been paid to this subject and every one of our cases in which a post-mortem examination was made was carefully examined in order, if possible, to find a primary bubo of the first order of the mesenteric or other intestinal lymph glands. But none was encountered. It appears that up to date the occurrence of intestinal plague in man has not been proved beyond dispute. Even where rats have been fed on plague-infected food, the disease is generally of the bubonic type (cervical or submaxillary bubo) with simultaneous or secondary plague septicæmia.

Another type of the disease which has been grouped separately, but which generally is not accepted as a type *per se*, is skin or

cutaneous plague. In our material we have not seen an example of this type, and it may be mentioned that cases classed as cutaneous plague have generally only been observed clinically and not studied post-mortem.

Muschold, in reviewing the literature on cutaneous plague, says:

The term cutaneous plague applies to those cases in which there exists at the beginning a (primary) plague vesicle, pustule, or carbuncle without marked involvement of the lymph glands. If in the further development of the disease the skin lesion does not spread, but the neighboring glands become more prominently involved, then it would be better to speak of cutaneous and bubonic plague, or still more preferably of bubonic plague with primary skin lesion.

The German Plague Commission among its clinical material had fourteen cases of cutaneous plague, all of which, however, were complicated by buboes; and the Austrian Commission likewise saw no case of this form without typical buboes. Only Kitasato has mentioned one case of primary plague carbuncle without buboes but with septicæmia. From these data it would appear that a separation into a group of those plague cases which show a marked reaction at the cutaneous portal of entrance of the virus is hardly justifiable and somewhat arbitrary. The extensive report of the Indian Plague Commission does not recognize a distinct cutaneous form of the disease.

Another type mentioned by writers is ambulatory plague or *pestis minor*. While such a group is admissible from a clinical standpoint, it has no proper place in a classification based strictly upon the pathology of the infection. Under *pestis minor* are classed those mild cases in which a swelling of some of the external lymphatics is generally observed, but in which there are no urgent clinical symptoms, and in which, in fact, a correct diagnosis may be arrived at only after more serious cases have made their appearance. These cases properly belong to the bubonic type. Our knowledge of them, even from a clinical standpoint, is very meager; from a pathologic one it is practically nil. While every case of *pestis minor* is ambulatory, every case of ambulatory plague is not necessarily one of *pestis minor*. Indeed we can report such a one in which the individual died very suddenly and where on post-mortem examination such profound plague lesions were found, quite aside from its fatal termination, as to remove it from the group of *pestis minor*.

## THE MORBID ANATOMY AND HISTOPATHOLOGY OF PLAGUE AS DESCRIBED IN LITERATURE.

The number of articles on plague which have appeared since the discovery of the specific micro-organism is very considerable. Most of the literature deals largely or exclusively with the clinical aspect, the bacteriology, the prophylaxis, or the serumtherapy of the infection, so that the number of contributions to its morbid anatomy and histopathology is comparatively limited. It is surprising to find, from a lecture delivered by Virchow in 1879, how little was then known of the pathology of the greatest scourge of the Middle Ages.

Virchow had no opportunity personally to study cases of the disease, and he therefore simply gives a review of the writings of the eighteenth and nineteenth centuries, up to 1879, drawing attention to the then prevalent contradictory views on the pathology of plague. From these he selected, in an admirably critical manner, those which indeed come nearest to the correct pathology as it is now known. Virchow's plague lecture in 1879 also contains this remarkable prophetic declaration: "To me the similarity of anthrax and plague is so great that I consider it very possible that we shall find an organism as the carrier of plague infection. However, an attempt to find it has heretofore hardly been made."

Aoyama, simultaneously with the bacteriologic work which led to the discovery of the plague bacillus, investigated the gross and microscopic pathology of the disease. He described the swelling of the infected lymph glands as brought about by a proliferation of their cells and he noticed the changes found in plague in the periglandular tissue. He stated that the spleen was always considerably enlarged, hyperemic, and soft, the kidneys and the liver somewhat increased in size and much congested, while the cells of these organs showed parenchymatous degeneration. The lungs are described as unchanged. The plague bacilli were found to be present in large numbers in the affected glands but rare or absent in the blood.

Yamagiwa's observations were made during the latter part of the plague epidemic in Formosa in 1896. While he had access to a considerable number of cases which he could study clinically, his pathologic material, owing to political reasons, was limited to three post-mortem examinations. Besides these he was able to obtain several glands extirpated *inter vitam* which he included in his microscopic studies. All three of Yamagiwa's cases were bubonic plague, one complicated by a metastatic dissemination of the bacilli in the lungs, spleen, and liver, or, as we would now classify it, a primary bubonic case with secondary plague septicopyemia. However, the summary of the morbid anatomy and histopathology, as given by Yamagiwa, while quite correct on the whole, does not apply to all cases of plague, as the investigation of a larger amount of material very clearly shows.

At the time of Yamagiwa's writings plague pneumonia had not yet been described by modern writers, nor was plague septicæmia

well understood. So the statement that all changes, except those of the lymph glands and the tissues of their immediate neighborhood, are generally insignificant, is untenable. We have among our own cases, some of pneumonic and septicæmic plague, in which the changes in the glands are quite insignificant compared with those in other organs, and of course this observation is at present not at all new.

It is very interesting to note that in Yamagiwa's third case, where the hemorrhagic edema and the swelling of the cervical and submental glands was enormous, and the consequent pressure upon the trachea very great, the latter suffered an incomplete fracture of its cartilages and became flattened out into a scabbard-like canal. The frequency and importance of submucous and subserous hemorrhages in plague were duly emphasized by Yamagiwa, and he calls attention to the fact that in the affected lymphatic chain the gland nearest to the point of entrance of the bacillus is more profoundly changed than are those farther away. However, this is not always the case. Other changes particularly mentioned are parenchymatous nephritis and cloudy swelling of the liver and heart muscle, acute swelling of the spleen, and edema of the lungs. The main histologic alterations described are degeneration of the renal epithelium with granular material in the tubules, cloudy swelling of the liver parenchyma cells, dilatation of splenic vessels with hemorrhagic infiltration, necrotic foci and the presence of plague bacilli, dilatation of pulmonary vessels with interalveolar blood extravasation, vascular dilatation, phlebitis and necrosis of the lymph glands and of the periglandular tissue. The extensive blood extravasation in the affected glands is explained in the following words: "The profound change in the walls of the veins, the great loosening (*Auflockerung*) of the substance of the vessel walls in consequence of cellular infiltration, brings about colossal blood extravasation inside and outside of the lymph glands."

The credit of having first lucidly and correctly described a form of plague which is now universally recognized as a separate and important type—plague pneumonia—belongs to Childe of the Indian Medical Service. Since his description of the pathology of plague pneumonia has not been given the prominence it well deserves, by several writers, it will here be quoted somewhat at length. Of course reference to a pneumonic form of plague had been made long before Childe's publication.

In fact, it had been well observed during the Middle Ages. During the great plague pandemic which decimated Europe between the years 1347-1350 pneumonic plague was very prevalent and Guy de Chauliac, the physician of Pope Clement VI, who observed the plague in Avignon, and who himself became very sick with it, distinguished two types and wrote: "*Pestis habuit duos modos. Primus fuit per duos menses cum febre continui et sputo sanguinis. Et isti moriebantur infra tres dies. Secundus fuit*



per residuum temporis cum febre etiam continua et apostematibus et anthracibus in exterioribus, potissime in subasellis et inguinibus. Et moriebantur infra quinque dies. Et fuit tante contagiositatis, specialiter quæ fuit cum sputo sanguinis, quod non solum morando, sed etiam inspicendo unus recipiebat ab alio." (Haeser: *Lehrbuch der Geschichte der Medicin*, 3 Aufl., Iena, 1882.)

Childe gives the following description of the first case in which he made a post-mortem examination: "The lungs showed much general engorgement and œdema, with sero-sanguinous frothy fluid in the bronchi, but no pus; the usual appearances of acute bronchitis were absent. There was one small pneumonic patch the size of a walnut, in the early second stage, situated below the apex on the front of the right lung, and two similar but smaller patches at the same part of the left lung. These patches stood out a little from the surface, and were airless, friable, sank in water, each was surrounded by a dark ring of engorgement, which merged into the healthy lung, and there was recent pleurisy over the pneumonic areas. All the other organs were examined and showed considerable engorgement, but no special lesion was observed. The cervical, the axillary, and the lumbar lymphatic glands were slightly enlarged. The left iliac slightly enlarged, red, and soft; all the other glands, including the bronchial, looked absolutely normal. Cultures made from the pneumonic lungs and spleen developed plague bacilli." Childe, in the same article, reports the clinical features of two cases of pneumonic plague—those of a physician and of his nurse—and then says:

"This form of plague is highly infectious, and probably has a large share in the spread of the disease, for in these cases the patient's sputum is practically a pure culture of the plague bacillus, and, as there is reason to believe that many of the cases are not recognized as plague at all, precautions are not taken by the patient's friends and the dangerous nature of the disease is not appreciated. I have no means of knowing how frequent this variety of plague has been in the present epidemic, but there is some evidence to show that a considerable number of cases have occurred.

\* \* \* With regard to the literature on this subject, I have not been able to find a published description of this variety of plague, but an allusion is made in the accounts of the Pali epidemic of 1836, and it is stated that the Astrakhan outbreak of 1877 was first regarded as croupous pneumonia or as typhus complicated by pneumonia. From the reports on the Hong-kong epidemic it appears that plague pneumonia did not occur there. There is just this to add: The usual definition of plague in works of medicine is: 'A specific fever, attended by bubo of the inguinal or other gland,' but it seems that such a form of words does not include all varieties of the disease."

In a later contribution on the pathology of plague Childe also takes up that of the common bubonic type, and states that the glandular lesion is chiefly at the site of the bubo and there are but slight lesions of the lymphatic glands throughout the body, but there are found engorgement or petechiæ, or hemorrhages in nearly all viscera, notably in the alimentary canal, especially the stomach and large intestine,

the kidneys, and bladder, the pericardium, pleura, and peritoneum, and with enlargement of the liver and spleen. In the septicæmic form there is general involvement of nearly all the lymphatic glands and lesions in the other organs similar to those found in the bubonic form. No bubo of the mesenteric glands was ever found. These glands were always examined, and, though changes might be found in them, they were always less marked and less distinct than plague glands found in other parts of the body. In short, there was no necropsy, which went to show that the plague bacillus had reached the stomach or intestines—for example, in food—and thence infected the mesenteric glands.

In his later contribution Childe describes the pneumonic form of plague as follows:

"In this form of plague the only marked evidences of disease are found in the lungs. The lymphatic glands and other organs are scarcely affected at all. In the lungs there was general engorgement, with considerable œdema, a reddened condition of the mucous membrane of the bronchi, but no marked evidences of bronchitis, and frothy watery fluid, sometimes blood stained, could be squeezed from the bronchi. (Pus in the bronchial tubes was only found on one occasion.) A number of pneumonic patches were found scattered through the lungs, varying in size from a pea to an egg. They were light pink or red gray in color, solid, airless, and sank in water. They were rounded in shape, and usually separated by a distinct ring of engorgement from the crepitant lung around. Some, instead of being pink, were of a deep blood color throughout and less solid, and some of these had a small, greyish, more solid center. Those of the patches which were situated on the surface of the lung were prominent, and projected distinctly from the surface whilst the pleura over them was roughened, and showed signs of early inflammation. These patches had, in fact, the appearance of the first and second stages of lobular pneumonia, but no patches were found which had passed on to the third stage of softening and breaking down. In a few cases larger masses of pneumonic lung than these were found and once about half the lower lung was found in this condition. Petechial hemorrhages were usually found on the surface of the lung; the bronchial glands were either enlarged, swollen, œdematous, soft, and distinctly engorged, or else they were small, and of the usual appearance, perhaps a little engorged. The remaining lymphatic glands throughout the body showed none of the appearances of either the bubonic or septicæmic form of plague; most of them looked absolutely normal, and the only noticeable change was that the axillary and sometimes the cervical chains were a little engorged."

Childe found large hemorrhages absent in plague pneumonia, but the usual subserous or submucous petechiæ and ecchymoses were present. This author describes the microscopy of the pneumonic form as follows:

"A section of lung tissue, apart from a pneumonic area, shows great engorgement of all large blood vessels, and of the alveolar capillaries as well, and patches of hemorrhage into the alveoli around these engorged vessels are seen scattered about. In a pneumonic area three zones can be made out. At the circumference there is intense engorgement of

all vessels including alveolar capillaries, the alveoli are full of blood and the hemorrhage is so intense that many of the alveolar septa are broken down, entirely absent, or represented by mere shreds. Within the circumference is seen a zone in which the alveoli are intact and are completely filled with well-stained cells, so that there is no interval between the alveolar wall and their contents, and in the center is one universal mass of similar cells, and the cellular infiltration is so extreme that the walls of the alveoli are scarcely visible. Such is the general arrangement of the pneumonic patch, although there may be alveolar hemorrhage in parts of either the middle or central zone. Under a higher power the alveoli of the circumference are seen to be completely filled with blood corpuscles, and a little fibrin or none at all, whilst the dense central mass of cells consist of catarrhal epithelium and leucocytes with some granular débris. Thus the pneumonic area has the appearance of very extreme lobular or catarrhal pneumonia. The walls of the bronchial tubes, as well as the large veins, show great engorgement and there are hemorrhages into the vein walls. Blood and catarrhal cells may be seen in the finer bronchi, but the bronchial mucous membrane is scarcely altered, there being at most a little cellular proliferation. There are the appearances of acute pleurisy over those pneumonic areas which project upon the surface of the lung, with hemorrhages beneath the pleura. The bronchial glands show engorgement of blood vessels, but in some cases these conditions are only slightly marked and the glands looked nearly normal. \* \* \*

"In cases of plague pneumonia the bacilli were seen in abundance in the pneumonic areas; they could be found in profusion amongst the catarrhal epithelial cells and leucocytes which filled the alveoli and terminal bronchioles, as well as among the blood corpuscles of the alveoli into which hemorrhages had occurred."

Childe also describes a case of plague septicæmia with secondary deposits in the liver, which in this particular instance was most peculiar; it was slightly enlarged and congested, as in the early nutmeg condition, and was stuffed throughout with small, yellow, rounded masses, varying in size from a pin's head to a pea. They were rather soft and friable, but not fluid, and there was no area of engorgement around them. They were found both on the surface and throughout the whole substance of the liver. They looked like necrotic foci and microscopically proved to consist of dense masses of plague bacilli with necrotic cells surrounding them.

It may here be mentioned that Bazaroff, working under the direction of Roux, first produced plague pneumonia experimentally in animals by introducing plague bacilli in their nasal cavities. The disease developed by experiments is described as a lobular or confluent broncho-pneumonia with secondary general septicæmia.

The German Commission distinguishes three types of plague: Bubonic plague, plague pustule of the skin, and plague pneumonia. Whether an intestinal form of plague exists the Commission is unable to decide; it did not encounter a case in the human material examined, though it succeeded in producing intestinal plague in rats and monkeys by feeding

them infected food. The Commission does not believe in the existence of a true primary plague septicæmia and its report states with reference to this subject:

"Primary plague septicæmia probably does not exist. At least our own Commission as well as the Austrian one, and other investigators, have found on post-mortem examination, in such cases in which the portal of entrance of the virus could not be ascertained, small hemorrhagic glandular foci, or a focus in the lung. These had in consequence of the indifference of the patients or in consequence of their occult location, escaped notice during life. Hence plague septicæmia is not a special type of the disease, but the generalization of a primarily local process. That it may then again lead to other secondary internal foci we have demonstrated in a case of plague meningitis."

Septicopyemic processes with pus metastasis, the commission believes to be due to a mixed infection, as is also the case in purulent abscess formation of the plague bubo. From this condition the commission separates a puriform softening of the bubo without abscess formation, which may occur in pure plague infection without the presence of other micro-organisms. The pathologic anatomy is described as follows:

The bubo is anatomically a larger or smaller tumor, which contains one or more enlarged lymph glands; these are rarely greater than a pigeon's egg. They are united into one mass by either œdematous or hemorrhagic connective tissue. The glands and the surrounding tissue show all degrees of inflammation, from simple medullary swelling to œdematous infiltration, bloody infraction, suppuration, and complete necrosis, according to the intensity of the process, the duration of the disease, and the single or multiple microbial infection. As is the case with the periglandular tissue, the neighboring fascia, the areolar tissue, the muscles, the sheath of the vessels and the nerves may likewise be included in the œdematous gelatinous or hemorrhagic infiltration; these structures may, as it were, become parts of the bubo. It is not so rare to find a bubo which extends from the inguinal glands to the cysterna chyli, from a cubital gland into the axillary space up to the vena subclavia or from the angle of the maxillæ deep into the thoracic cavity. In such extensive cases the peripheral glands show a milder, the more central ones a more profound degree of inflammation and destruction; while the younger stage of the process is present in the latter, the older one in the former. The anatomical findings in the plague-infected lung can be described with few words. In the lobular form, we generally have quite an extensive process with its favorite seat in the lower lobe. This lobular type of pneumonia is characterized by a peculiar mixture of the different stages of hepatization and by an accompanying serous catarrh. In the hybrid types in which old tubercular foci and fresh plague inflammatory processes are mixed, the picture becomes still more varied. Twice we saw in croupous foci, necrosis and hemorrhagic infiltration of the center to such an extent that expulsion of larger masses

of lung tissue and profuse hemorrhages might have occurred at any moment. The bronchial glands, in some cases of plague pneumonia, appeared like the external primary buboes, while in other ones, more extensive changes were lacking. Besides the primary lesion one regularly finds in plague cases, even in those which have died in the second or third week from complicating affections, blood extravasations into the various internal organs. Rarely have such hemorrhages taken place into the skin, the subcutaneous connective tissue, or into the muscles. However, petechiæ in the mucosa of the intestinal tract, frequently confined to the fundus of the stomach and to the cecum, are often found. These hemorrhages usually vary from the size of a mere point to that of a lentil, or sometimes they may even be larger. They often have become confluent stripes, and appear as such on the mucosal folds. In a few cases such punctiform or linear hemorrhages are seen from the pharynx to the anus. Where old ulcerative processes are present the hemorrhages frequently appear around such lesions. One finds petechiæ regularly in the pelvis of the kidneys, more rarely in the renal capsules, in the gall bladder, in the serous membranes of the heart, the lungs, the liver, etc. The lungs, the testicles, the sheath of the nerves, the dura, the uterine mucosa, the placenta, are in some cases the seat of more extensive hemorrhages, even if far distant from the seat of the primary bubo.

All these hemorrhages are not the direct effect of the bacteria, but more probably the consequence of intoxication. In proof of this view the Commission reports that it obtained three fetuses from plague patients. All three presented numerous hemorrhages but were found absolutely germ free. The Commission further states that it generally found marked parenchymatous degeneration in the internal organs, generally enlargement of the spleen and swelling and hyperemia of the lymph glands aside from those affected by profound hemorrhagic infiltration.

The German commission does not report any microscopic examination of tissues from plague cases.

Albrecht and Gohn,<sup>1</sup> of the Austrian Plague Commission, have introduced the terms primary and secondary buboes. Primary buboes, according to them, are those which are formed by the introduction and the extension of the micro-organisms along the lymph channels, while a secondary bubo is always the result of the propagation of the virus by the blood current. The chief form of plague is denominated by them "septicæmic hemorrhagic." It is characterized by a primary bubo, located most frequently in the inguinal, axillary and cervical regions, about which there occurs a hemorrhagic œdema, and at greater distance hemorrhages into the organs. The spleen is swollen, the general lymph glands are enlarged, and the parenchymatous organs show degenerative changes. The primary bubo may be entirely lacking, the swelling of the lymph glands may be inconspicuous, and the hemorrhage may be the only pronounced sign.

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<sup>1</sup> Albrecht and Gohn's original report has not been accessible, and we therefore quote mostly from Musehold, Flexner, and others who have freely referred to the work of the Austrian commission.

A second form of the pest which they describe is the septicopyemic. In it embolic foci are present in the lungs, the liver, and the kidneys. A third one is the primary pest pneumonia, which is a confluent lobular pneumonic process, usually attended with noticeable lymphatic enlargement. The common portal of entrance of the bacilli is the skin, but only exceptionally can the precise point of infection be discovered, the demonstration of the place and the mode being indicated by the location of the primary bubo. A single instance of purulent meningitis, due to the pest bacillus, was encountered by the Austrian Commission. The invasion of the blood takes place always from the primary bubo or from the lungs, as a primary blood infection does not exist. The primary bubo may be so small that it cannot be discovered clinically and is found anatomically only after careful and prolonged search. In foudroyante cases the formation of a bubo may fail altogether. The primary bubo is distinguished by destruction of the lymphatic parenchyma, necroses, and hemorrhages, and (in the case of mixed pyogenic infections) by suppuration. A similar condition is found in the surrounding cellular tissue. Bacilli are present in great numbers. The secondary buboes show, on the other hand, uniform hyperemia, occasionally hemorrhages, and, in more protracted cases, medullary swelling. The primary buboes of the second order approach one or the other type, depending upon their distance from the gland primarily affected. The multiple hemorrhages are not the result of the action of toxines elaborated at a distance, but are caused directly by bacilli which may always be found in the neighborhood. Parenchymatous and fatty degeneration of the heart, the liver, and the kidneys occur commonly. Splenic tumor is a constant occurrence. The spleen shows marked changes. The pulp is distended with blood and contains many poly-morpho-nuclear cells. The follicles are but little altered, but the trabeculae are swollen and homogeneous. In some instances the endothelial cells of the pulp have proliferated and desquamated. When very great numbers of bacilli are present miliary necroses may occur. The bacilli are very abundant in the pulp, more scanty in the follicles; sometimes they may be contained within cells. In the pyæmic form of the disease foci are found in the liver, the lungs, the kidneys, the spleen and the musculature. In about one-third of all the cases of plague secondary pyococcal infection has taken place.

The primary pneumonia appears in the form of a lobular consolidation, which, when foci are numerous and confluent, may produce lobar solidification. Bronchitis is present. The bronchial lymphatic glands present appearances of primary, the others of secondary buboes. In addition to the primary, two other forms of pest pneumonia are recognized, one metastatic, which appears as multiple and larger foci, seated beneath the pleura, the other as an aspiration pneumonia, from the aspiration of infected material derived from buccal buboes. In plague pneumonia one generally sees shining through the lungs, fine, yellow and red markings or spots, which are produced by yellowish points or stripes on a red background. The picture resembles the one presented by plague lymph glands rich in bacilli. In the lungs this appearance is produced by enormous masses of bacilli contained in the alveoli. The cut surface shows a picture

similar to that seen on the pleural surface; much viscid exudate can be scraped from the surface. The plague foci in the lungs are surrounded by a hemorrhagic ring in an œdematous area. The alveolar septa are broadened. Microscopically they consist of a tissue which stains well with eosin, and which contains a few cells or cell nuclei or red blood corpuscles. The finer changes in the lymph glands, according to Albrecht and Gohn, consist in necrosis of the vessel walls and in a very peculiar coagulation of blood constituents. The more resistant vessels are generally enlarged, their walls somewhat thickened. They are either uniformly thickened and homogeneous or more frequently composed of solid bands of fibers which stain deeply with eosin. In the interior of a vessel with such changed walls, one finds a similar reticulum, sometimes consisting of fine filaments, sometimes containing irregular masses or lumps. Threads penetrating the vessel walls are in connection with the threads in the interior. The picture reminds Albrecht and Gohn of the coagulation necrosis observed in the epithelial layers of a diphtheritic membrane. Fibrin, however, is either not found at all or else sparingly.

Wysokowitz and Zabolotny, members of the Russian Plague Commission, studied the disease in Bombay; they made twenty-seven autopsies and most of their cases were those of bubonic plague. Six were of the primary plague pneumonic form. In the bubonic cases they also found all the other glands more or less swollen; however, these were less affected than the primary bubo, which was generally found to be very hemorrhagic. Plague pneumonia is classified by them as a bronchopneumonia, with a tendency of the foci to become confluent in the more protracted cases. A whole lobe was never found involved in the pneumonic process. Hemorrhages in the gastric and intestinal mucosa were present in many cases of all types, and the mesenteric glands were usually enlarged; in one case the liver showed necrotic foci. The Russian authors, neither in their clinical nor in their post-mortem researches, saw a case which would suggest the intestines as the portal of entrance of the plague virus.

The Anglo-Indian Plague Commission, whose medical members were Fraser and Wright, has published in five volumes the most extensive report on the great modern plague epidemic of India. It divides plague into four types, namely, (1) bubonic, (2) septicæmic, (3) pneumonic, and (4) *pestis minor* or *ambulans*, and elaborates upon the classification as follows (Vol. V., p. 53):

(1) Plague, in its most typical variety, takes the form of bubonic plague. In this form of plague the bacteria are carried by the lymph stream into the lymphatic glands, in particular into the lymphatic glands of the groin and the axilla—less frequently into those of the neck. The bacteria multiply there, and excite a considerable amount of swelling and inflammation, which manifest themselves in the form of a bubo. The development of this bubo is often associated with severe pain. Following closely upon—more rarely preceding—the development of the bubo, constitutional symptoms set in. They consist in malaise, headache,

and fever, frequently accompanied by collapse and vomiting. When the bacteria have grown through the meshes of the lymphatic filter, they are carried on by the lymph stream into the blood. The disease then becomes septicæmic.

(2) Distinguishable clinically though, from the point of view of the pathologist, not sharply marked off from the secondary plague septicæmias just described, are the cases of plague commonly spoken of as septicæmic, in contradistinction to bubonic cases. These are the cases where, owing to the more rapid passage of bacteria through the lymphatic filter, and possibly to a greater production of bacterial poisons, the constitutional symptoms precede and overshadow the local symptoms, the disease being in most cases rapidly fatal.

(3) In the third form of plague, first bacteriologically established by Captain Childe, I. M. S., plague bacilli invade the lungs and give rise to pneumonia, death occurring in most cases within a few days after the patient has been attacked. Owing to the absence of buboes, the pneumonic form is often classed, along with the septicæmic form, in the category of nonbubonic plague.

(4) In addition to the three main types of plague which have been described above, an abortive form of bubonic plague comes under observation. This is technically known as *pestis minor*, or *pestis ambulans*. It can not be doubted that in these abortive bubonic cases the bacteria are, as in the case of ordinary bubonic plague, carried to the lymphatic glands, but they are held back there, the disease stopping short of the septicæmic stage. In correspondence with this the constitutional symptoms are very light. Indeed in certain cases not only the constitutional, but also the local symptoms may be so slight as to be, except for their pathological interest, almost undeserving of attention. Such cases appear to be extremely common among persons who have been much exposed to the infection of plague and are characterized by sensations of numbness and tingling, or by neuralgic pains, which in many cases are associated with the development of spotty glands in the armpit and the groins. We may, however, remark here that the whole question of *pestis minor* urgently requires to be more fully elucidated.

From very extensive data the Indian commission has compiled the following summary of the pathology of plague:

Caste and other prejudices of the natives, which were consistently respected, have limited the number of post-mortem examinations relatively to the large mortality from the plague in India. Descriptions of the post-mortem appearances have, however, been laid before us, which together amount to a considerable total, and are sufficient to clearly establish the more important pathological features of plague. References may specially be made to the reports of Dr. Choksy; Captain Childe, I. M. S.; Dr. Dyson and Captain Calvert, I. M. S.; Captain Thomas, I. M. S., and Captain Leuman, I. M. S., and to the evidence of several of these gentlemen and also of Captain Wilkinson, I. M. S., Major Evans, I. M. S., and Captain Elphick, I. M. S.



*Pestis minor*.—Death from *Pestis minor* probably never occurs, at any rate, no description of the pathology of plague deals with this type.

*Pestis major, lymphatic system*.—(a) *Buboes*.—The appearance of the buboes was characteristic. As we have already stated, they varied much in size and to a less extent in number. For the most part they consisted of enlarged lymphatic glands surrounded by extravasated blood and serum, which in many instances extended widely and deeply into the neighboring areolar tissue, and often penetrated into the substance of the muscles. Sometimes only one gland was included in a bubo, but more frequently there were several, and at times an external bubo was directly connected with one involving deeper seated neighboring glands, and when a femoral bubo extended inwards so as to be continuous with one involving the iliac glands. The swollen glands and the surrounding tissues were often “matted together—so that it was difficult when once cut into it (the bubo) to be quite sure which was gland and which was surrounding tissue.” The affected glands were round or oval in shape, and they varied in size from that of a pea to that of a walnut. On section, they were seen to be much engorged with blood, of a light red or deep purple color, and of firm consistence in some cases, but soft and almost diffluent in others. When the bubo was in the groin, the limb of the same side was usually swollen and œdematous; when in the axilla, the serous effusion and hemorrhagic exudation was sometimes so great as to form a swelling involving the whole axilla and extending down the inner aspect of the arm to the elbow, and down the side of the chest nearly to the lowest ribs; and when in the neck a large swelling frequently resulted, which pressed upon the larynx, trachea and cervical nerves and blood vessels, and thus produced the dyspnoea which was so conspicuous a symptom in those cases. As buboes in the groin and axilla frequently pressed upon or surrounded the large blood vessels in these regions, the œdema in the corresponding limbs is readily accounted for.

It has been pointed out by Dr. Childe that in axillary buboes and occasionally in chains of enlarged glands along the course of the iliac artery and veins, the extravasated blood may be continuous with blood in the interior of the veins, thus forming “a direct path for the passage of the plague bacillus from the gland to the lumen of the vein, and so into the general circulation.”

In a few cases of *Pestis major*, no pathological changes were found in other lymphatic glands than those in connection with which buboes had formed; but in most cases, many other glands, and especially the internal glands, were affected. The changes in them, however, were relatively slight, for they consisted only of enlargement, and of either moderate or great congestion, a section of the gland in the latter instance showing much engorgement with dark blood. In individual cases, many or few of the glands were affected; but indeed no lymphatic gland, whether internal or external, seemed to escape involvement, for these changes were observed in various groupings, in the bronchial, mesenteric, peritoneal, iliac, lumbar, trochlear, popliteal, and other glands.

*Lymphatic vessels.*—In most cases, the lymphatic vessels showed no pathological change, and only in a few were they observed to be congested and swollen, and that only close to the bubo.

*Alimentary system.*—The pharynx and the tonsils were greatly congested, the latter being enlarged and occasionally in a state of follicular inflammation. This congestion usually extended down the œsophagus, and in some cases hemorrhages were found in its walls. The stomach was almost invariably engorged with blood, and both minute and considerable hemorrhages were present in the mucous membrane. These hemorrhages have been classified by Captain James, I. M. S., as follows:

“A mild form in which, on holding the coats of the stomach up to the light, the course of the smaller vessels was found to be picked out by extravasations which also formed small arborescent patches on the mucous surface, or perhaps only reddened the edges of the rugæ.

“A severe form in which there were more or less extensive patches of hemorrhage into the submucous tissues or even into the stomach cavity.

“Distinct numerous petechiæ with definite circular outlines and varying in size from that of a pin’s head to that of a split pea. In one case the petechiæ were very numerous and covered nearly the whole of the mucous surface of the stomach. The appearance was so striking that it reminded one of the rash seen on the skin in a severe case of purpura.”

Similar appearances have been observed in the intestines. Congestions and hemorrhagic extravasations were most frequently seen in the large intestine and rectum, and less frequently in the small intestines. Occasionally Peyer’s patches and the solitary follicles were observed to be swollen. The liver and the spleen were enlarged, the latter being sometimes two or three times the ordinary size. Petechiæ were frequently present on the surface of the liver, and its substance was engorged with dark blood, and was soft and friable, indicating degenerative change. The spleen also was generally in a state of acute degeneration, soft and pulpy, and in some cases almost diffuent. On section, it was brick red or deep chocolate brown and always greatly engorged. The gall bladder usually contained bile, and occasionally there were petechiæ on its mucous lining. The kidneys were also much enlarged and engorged with blood, and presented the characteristics of acute parenchymatous degeneration. Minute hemorrhages were sometimes observed on the surface, and petechiæ and coagulated blood in the pelvis and calices. Extensive hemorrhagic extravasation has also been found outside the kidneys, which were then found “lying in a bed of blood.” The ureters and bladder were engorged, and petechiæ were frequently present on their inner surfaces. Besides engorgement, no important change was observed in the supra-renal capsules or thyroid gland, and the genital organs presented a normal appearance. The peritoneum was considerably engorged, but, above all, hemorrhages, often of large size, were found in many parts, as in the mesentery, in the retro-peritoneal connective tissue, on the under surface of the diaphragm, and over the spleen, liver, kidneys, and intestines.

*Circulatory system.*—The blood was dark and fluid, and gave the impression that it did not coagulate well. The pericardium generally contained

more fluid than usual, which was sometimes blood stained; and minute hemorrhages were found in both its vesical and parietal portions. The myocardium was generally soft with many muscle fibers undergoing granulo-fatty degeneration; and the right ventricle was always dilated while in many cases there was also dilation of the other cavities of the heart. The walls of the larger vessels appeared normal, but those of the veins were engorged, and minute and large hemorrhages were frequently observed beneath the inner coat. Dr. Childe found that when a large vein was included in a bubo, hemorrhage into its walls was constantly seen, so that the extravasated blood in the gland itself, in the areolar tissue outside, and in the walls of the vein was continuous.

*Respiratory system.*—The larynx was in all cases affected and in a few instances there was hemorrhage beneath its surface. In cases of cervical bubo, œdematous swelling involved the soft structures of the larynx and the aryteno-epiglottidian folds. The bronchial tubes were also congested and swollen, and in many cases contained blood-tinged frothy fluid; but the trachea was merely congested. The lungs were engorged with blood and with serous fluid; occasionally small hemorrhages were found in the lung substance, and when the lungs were cut into much sero-sanguinous fluid escaped. When pneumonia or broncho-pneumonia had occurred as a complication, the pathological changes produced by these diseases were also present. The pleural cavity contained blood-stained or clear fluid. Sub-pleural hemorrhages, sometimes of large extent, were found on the parietal, visceral and diaphragmatic pleura and occasionally there was evidence of fibrinous inflammation. Hemorrhages were sometimes present in the anterior and posterior mediastina.

*Nervous system.*—The dura and pia mater of the brain, as well as the coverings of the spinal cord, were congested, and in a few instances extravasations of the blood were found on the dura mater. The brain substance and spinal cord generally presented a healthy appearance; but occasionally congestions and œdema were present, which involved likewise the choroid plexuses. No pathological change has been observed in the nerve trunks.

*Bones, joints.*—It has further been noted that the marrow of the long bones is red and congested as in other infectious fevers, and that evidence of an infective inflammation is found in the fringe-like processes of the synovial membrane of the knee joint.

*Intense or septicæmic type of plague.*—In those cases in which the plague virus or toxin is in the patient widespread from the beginning of the illness, so as early to produce a general poisoning, whether septicæmic or toxæmic, the pathological changes, as might be expected, are much the same as in the more severe cases of *Pestis major*. Some observers, however, believe that pathological differences occur to distinguish this form of plague, and to serve, along with the symptoms, as a justification for the establishment of a so-called septicæmic type of the disease. They consist of the absence of buboes having the characters above described, and of a widespread involvement of glands, with distinctive changes in several of them. Although the lymphatic glands are always affected, in place of the affection consisting of one or, more rarely, of several groups of glands

being enlarged and surrounded with sero-sanguineous extravasation, while the other glands are either normal or merely enlarged or congested, in this, the so-called septicæmic form, the affection of the glands shows itself as a general involvement of all, or nearly all, of the lymphatic glands of the body, although in many instances the affected glands were chiefly those of the mesentery. In no case, however, did the involvement proceed to the formation of the characteristic plague buboes, but only to a moderate degree of change, practically restricted to the glands themselves, but still displaying in several of them certain distinctive features. These were moderate enlargement and œdema without much congestion, the glands being pink in color, firm and rounded, and with a soft interior, often possessing here and there small areas of softening surrounded by firm substance. Several of the affected glands may be thus modified, while others of them are merely enlarged and engorged with blood, thus resembling the less affected glands of ordinary *Pestis major*. Excepting the lymphatic glands, the parts that were affected showed essentially the same pathological changes as in the bubonic variety of *Pestis major*, but usually the number of parts affected was smaller and the degree of change in them was less.

*Pestis pneumonica or pulmonalis, or primary plague pneumonia.*—Inflammation of the lungs occurs, as already stated, with considerable frequency during the course of the plague, and it then becomes a serious complication. It also occurs so early in the disease as to justify the belief that the plague virus had affected the lungs either primarily or coincidentally with the more general affection of the body, thus constituting a form of plague which is distinguished as primary pneumonic plague. When contrasted with those occurring in *Pestis major*, the pathological changes elsewhere than in the lungs are less intense. While those in the lungs are more intense. The lymphatic glands are only slightly affected, and external buboes having the characteristics seen in *Pestis major* are seldom, if ever, encountered. Congestion and enlargement of organs and even hemorrhage in mucous and serous membranes may be present, but they do not assume the proportions attained in *Pestis major*. On the other hand, the lungs are conspicuously affected. The whole substance is engorged, the large as well as the small blood vessels being distended; and hemorrhagic zones are seen scattered throughout the lungs, filling the alveoli and often breaking down their walls. Within the hemorrhagic zones are areas in which the alveoli are completely filled with leucocytes, epithelial cells and granular debris, constituting, with the surrounding zones of hemorrhage, blood-congested areas of catarrhal pneumonia. In these areas, as well as in the fluid matter contained in the trachea and bronchi, plague bacilli are abundantly present. Greyish necrotic patches have also been found containing large numbers of plague bacilli. The bronchi are engorged with blood, and catarrhal cells are found in their terminations. Over affected areas at the surface of the lungs, the pleura may be acutely inflamed. In most cases, the bronchial glands were congested, and there was a little hemorrhage into the gland substance; but in some cases, their appearance was normal.

While, however, a catarrhal inflammation of lobular distribution has most frequently been regarded as the characteristic type of primary plague pneumonia, several observers have denied its existence, and have asserted that croupous (lobar) pneumonia is the form which most frequently occurs. Major Evans, I. M. S., and Captain Elphick considered that all cases of typical plague pneumonia come under the latter category, and Major Jones expresses the opinion that "lobar pneumonia is common." Major Evans stated that the pneumonia is distributed in small patches, constituting lobular areas, only when the inflammation has not advanced far; but that it is lobular to the extent of involving a whole lobe or the greater part of a lobe when the lung inflammation has advanced further. Captain Elphick, I. M. S., described several autopsies in which individual lobes or even an entire lung were consolidated, and he stated that "every case of pneumonic plague examined showed lobar condensation." It may further be stated that in many cases only slight changes were found in the bronchi. It is therefore possible that the pneumonia is lobular in patients who have died at an early stage of the disease, and lobar in those who have survived to a later period; or, otherwise, that lobar pneumonia occurs when the toxin is most virulent and most widely distributed throughout the lung, and lobular pneumonia when it is less virulent and less widely diffused.

The microscopic examination has mainly shown general dilatation and engorgement of the veins and smaller blood vessels and numerous capillary and larger hemorrhages in almost every structure and organ of the body.

*Indian Plague Commission's summary of pathological conditions.*—"The distinctive pathological changes produced by the virus of plague would therefore appear to consist of universal dilation and engorgement of veins and smaller blood vessels, with hemorrhages, both minute and of large amount, in nearly every part of the body, and of enlargement of the lymphatic glands, with œdema and hemorrhage in the surrounding tissues, generally mainly implicating the external glands, but occurring likewise throughout the body and involving in a series of cases the entire system of lymphatic glands. In the lymphatic glands, the characteristic conditions are largely explainable by vascular changes, and even in the pneumonia of plague, vascular dilatations and hemorrhagic extravasations give a special character to the lung inflammation. In no other infective disease are these features represented, but it is of some interest to note that the vascular changes, and especially the prevailing and characteristic tendency to extravasation of blood in almost every part of the body, are closely reproduced in toxæmia caused by the organic poison secreted by the venom glands of several species of serpents such as the black snake (*Pseudechis porphyriacus*) of Australia."

Flexner, who examined six cases of plague in San Francisco, besides giving a summary of the morbid anatomy, reports more fully on the microscopic changes of the lymph-glands and of the spleen. He states that in the primary bubo the separation into the medulla and cortex has been effaced, that masses of lymphoid cells still exist but that they do not compose typical structures. Remains of cell forms, nuclear fragments,

shadows of red blood corpuscles, and plugs of finely granular structure are seen filling spaces which suggest preformed vessels. Hemorrhages exist in the medullary and cortical parts. The bloodvessels are commonly thrombosed. The thrombi consist of cells, both mononuclear and polynuclear and fibrin. The walls of the smaller vessels often are hyaline and structureless. Fibrin stain shows a fine network of fibrin about the vascular walls, occurring partly within the lumen, partly within the wall, and partly beyond in the perivascular tissues. Larger vessels show instead of the fibrinoid transformation of their walls, destructive and infiltrative changes. The intimal and medial coats contain an increase of cells and many cell fragments. This infiltrative condition is especially marked in the middle coat. That many of these cells are polymorphonuclear is shown by the bizarre forms and the staining properties of the nuclei. The periglandular structures are extensively infiltrated and usually show necrosis as well. The infiltration is partly cellular, partly fluid, along with which fibrin is perhaps invariably present. The œdema and fibrin are found chiefly in the coarse fibrous septa of the adipose tissue; the cells occupy the meshes of the fat cells. Bacilli are abundant in countless numbers within the swollen glands and in the periglandular tissues. They occur in continuous growth throughout the glands, occupying every available space; they completely occlude many blood vessels or, mixed with definite thrombi, compose a considerable part of the plugs. Moreover the walls of the blood vessels contain masses of bacilli having grown within the vasa vasorum and the lymph spaces. The adventitial coats of veins and arteries are especially rich in such growth of bacilli. In the primary buboes of the second order the changes are all much less advanced and marked.

In a case of tonsillar infection changes similar to those described in the primary bubo of the first order were observed. The presence of cells resembling plasma cells is mentioned and many of these were observed to be phagocytic. The spleen, in Flexner's six cases, was found moderately enlarged, somewhat diminished in consistency, color deeper than normal. The pulp is described by the author as swollen, the swelling being the result of cellular proliferation, cellular infiltration, and œdema. The proliferation especially affects cells closely united with the veins and surrounding the trabeculae. These cells have reticulated nuclei, placed excentrically, and a fair allotment of protoplasm, taking the blue thionin stain. The cells are often polyhedral rather than round. They have a close affinity to plasma cells. The lymphoid cells are increased, but to a less extent than the cells just described. The vascular and other spaces in the pulp contain an increased number of red corpuscles. In the same spaces occur large cells of two kinds. One is a giant cell with single, lightly staining, reticulated nucleus and a moderate amount of protoplasm, and resembling the large, mononuclear, marrow cell with which it is probably identical; it is not phagocytic. The other is a much smaller cell, three to four times as large as the marrow cells and is highly phagocytic.

The macrophages englobe white cells—both mononuclear and polynuclear—but rarely red blood corpuscles. They occur at times within the larger veins, especially such as exhibit the subintimal cellular proliferation to be described. The polymorphonuclear cells in the pulp exhibit great variation in form and many would seem to have been in a state of active migration when the tissue was fixed. They show great variety of form, such as is seen in actively motile cells, and they would seem to be moving in numbers in the pulp. Fibrin is found among the pulp cells and in the fluid, and many bacilli are present.

The Malpighian bodies are increased in size, this being due to the multiplication of the lymphoid cells, and, to smaller extent, of epithelioid cells. The latter do not occupy the centers of the nodes, but are few in numbers and placed peripherally. Their nuclei are large and vesicular, rarely a cell contains two nuclei. Degeneration of cells is uncommon, very few fragmented ones being visible. Rarely small islands of fibrin are present in the nodules.

The blood vessels show two kinds of change. The arteries, chiefly those of the Malpighian bodies, have hyaline walls; the veins of all sizes frequently show subintimal cellular proliferation. The cells in the intima are mononuclear and more rarely polynuclear elements that form a continuous, although not uniform, investment or appear as isolated projections into the lumen of the vessel. Above these cells the displaced endothelial cells can usually be detected. Bacilli are very numerous, especially in the pulp. They also completely occlude small blood vessels, and within the trabeculae, probably lymphatics. However, since the richest growths of bacilli are often unassociated with reactions, it is highly probable that they may have taken place post-mortem.

Calmette and Salimbeni made observations on plague during the last Oporto, Portugal, epidemic, and they describe the macroscopic and some microscopic lesions as follows: The buboes may be single or multiple, in most cases they were multiple. They consist of one or more glands of the same region. The former are increased in size in consequence of a hemorrhagic inflammation which extends into the periglandular tissue and sometimes into the overlying skin, producing phlyctenae which may contain plague and other bacteria. Microscopically one finds cellular debris, masses of chromatin, few leucocytes, and many plague bacilli. In the most profound rapidly fatal cases there are extensive hemorrhages, however, when, death is delayed and is brought about by complications, one finds that the contents of the bubo are true purulent material with few plague bacilli. The authors also described the so-called cutaneous plague type, of which, however, they saw very little in Oporto. Once they observed a case which began as an oedematous, very intense inflammation of the skin of the hand and the forearm and progressed to dark discoloration and necrosis. In all three cutaneous cases which were observed a bubo developed in the neighborhood of the superficial plague lesion. Skin lesions in the shape of petechiae, ecchymoses, pustules, and hemorrhagic vesicles were also observed in typical primary bubonic plague. The two authors observed a case which resembled hemorrhagic smallpox. In the internal organs congestion of the intestinal mucosa, swelling of the mesenteric glands,

fatty degeneration and necrosis of the liver and an enlarged spleen sometimes of good consistency, but more frequently soft and friable, were found on post-mortem examination. The kidneys showed evidence of parenchymatous degeneration, sometimes with hemorrhagic foci; such were also exceptionally seen in the bladder. The heart showed subepicardial hemorrhages; endocardial inflammation or valvular changes were not seen. Once a meningitis and once a meningo-encephalitis was observed. In all grave forms of the disease the lower and posterior portions of the lungs were found hypostatic. A pure case of primary plague pneumonia was not seen at autopsy.

Jennings, in his *Manual of Plague*, gives a summary of the pathology and morbid anatomy of the disease, in which he states that discoloration, distinct from post-mortem lividity, caused by small or large subcutaneous blood extravasation is almost invariably present in different situations. Papules, vesicles, or pustules may exist, also scabs or unhealthy ulcers. The skin over buboes may show a necrotic appearance, or necrosed patches of skin or large sloughing ulcers may also be present. Diffuse swelling around the buboes occasioned by infiltration is often observed. The lymphatic vessels, except those associated with the buboes, are seldom involved; occasionally, however, a more extensive, widespread lymphangitis may be present. The glands may simply be enlarged, congested, or engorged, or they may show a profound hemorrhagic condition. The hemorrhages are often extended into the periglandular tissue and they may infiltrate the whole neighborhood. Glands distant from the bubo are generally swollen, congested, and engorged. Plague bacilli are abundant in the pulp of the affected glands, but generally disappear after marked softening or true suppuration have appeared. In septicæmic plague the glands show very moderate changes only. In the gastrointestinal tract congestion of the mucosa and œdema of the visceral walls are generally observed, and petechiæ in the stomach and large intestines, and to a lesser extent in the small intestines, also occasionally more extensive hemorrhages in the submucous tissue of the stomach occur. The solitary and the agminated glands are swollen and congested, but never ulcerated; the retroperitoneal and mesenteric glands are generally in the same condition and often hemorrhagic. The spleen is much enlarged and subcapsular hemorrhages make the surface lumpy and uneven. The liver is increased in size and engorged, and sometimes presents a nutmeg appearance; occasionally yellow necrotic patches are found scattered throughout the organ. Petechiæ are common on the surface. The kidneys are generally intensely imbedded in extravasated blood; petechiæ are common on the surface, also in the pelvis and calices; sometimes coagula are found in the former. Glomeruli are engorged, all the blood vessels distended and the epithelium of the tubules generally in a state of parenchymatous degeneration. The genital organs are generally unaffected, but in cases in which abortion has occurred, the subinvolved uterus and the ovaries are engorged and œdematous. The lungs are generally engorged. Frequently hemorrhages are found in the lung substance or on the surface, scattered over the pleura, or in the mediastina. When the lungs are primarily involved or secondary pneumonia



supervenes, the walls of some of the alveoli are broken down by the severity of the hemorrhages and patches of catarrhal inflammation, varying in size, are scattered throughout the lungs. These patches are surrounded by belts of engorged lung tissue. They may coalesce into larger patches. Sometimes a whole lobe may thus be consolidated. The patches at first are red and later on become gray; they are quite solid and do not float on water. The air cells in the affected areas are filled with an accumulation of epithelial elements, granular debris, cells resembling leucocytes, intimately mixed into a gelatinous mass in which plague bacilli, often in association with diplococci or streptococci, abound. The vessels in general are dilated, the heart sometimes unaffected, more frequently soft, flabby and friable. In all cases the right side of the heart is dilated and contains post-mortem coagula.

#### A STUDY OF TWENTY CASES OF BUBONIC PLAGUE.

The material which forms the basis of the original work of this bulletin consists of twenty cases of plague occurring in Manila and upon which autopsies were performed by the writer during the period of time from February 19 to September 8, 1904. These cases were without exception fully examined anatomically on the post-mortem table, and also by cultural and histologic methods. In the majority of the cases, in addition, animal experiments were performed with the organisms isolated. One case which was not completely studied has been included, because it showed the hyaline fibrin thrombosis of the glomerular vessels which is so characteristic in plague.<sup>1</sup>

The histologic material was in all cases at the time of the autopsy immediately fixed in Zenker's solution and was subsequently embedded in paraffin and sectioned. In addition, in one case the material was fixed in Flemming's solution. The stains employed in the study of the sections were hematoxylin and eosin, eosin and alkaline-methylene-blue, carmine and Weigert's fibrin stain, dilute carbol-fuchsin and occasionally other stains. Dilute carbol-fuchsin, which we found the most useful dye for smears from the organs, is not very satisfactory in the treatment of sections, stained with a view of studying the distribution of the plague bacillus, nor did

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<sup>1</sup>The number of cases upon which necropsies were performed during the above-mentioned period of time has been in excess of twenty; but some of them were not considered in this report because of the greatly advanced putrefactive changes, which excluded a satisfactory anatomic and histologic examination, or on account of the late hour in the day in which, for the sake of an immediate diagnosis, the necropsy had to be hurriedly performed, in consequence of which a careful anatomic study became impossible.

we obtain any good results with a modified Romanowsky dye. Eosin and methylene-blue is the best for exhibiting the plague bacillus, but in using this stain one must be careful in decolorizing, or else too many plague bacilli lose the stain and fallacious conclusions may be arrived at. This dye, as a rule, fades quickly in the Tropics in an atmosphere saturated with moisture, and hence the sections treated with it must be examined without delay, and in a later reëxamination, recoloring frequently becomes necessary.<sup>1</sup>

The twenty cases to be reported below in detail have been classified under the following six groups:

	Cases.
Group I. Primary uncomplicated plague.....	11
II. Primary bubonic plague with secondary plague septicopyemia .....	4
III. Primary bubonic plague with secondary plague pneumonia..	1
IV. Primary uncomplicated plague pneumonia.....	2
V. Primary plague pneumonia with secondary plague septicopyemia .....	1
VI. Primary uncomplicated plague septicæmia.....	1
<hr/> Total .....	<hr/> 20

#### GROUP I. PRIMARY UNCOMPLICATED BUBONIC PLAGUE.

[Eleven cases.]

##### CASE NO. 1. LEFT INGUINAL BUBO.

[Necropsy Protocol No. 1009. Post-mortem examination July 27, 11 o'clock a. m., about eighteen hours after death, on the body of C. S., a male Chinese, 36 years old, from 217 Santo Cristo. Died July 26 at 4 o'clock p. m.]

Body of a well-developed, fairly well-nourished, male Chinese about 35 to 40 years old. Post-mortem rigidity not very marked, surface quite cyanotic; post-mortem lividity has made its appearance all over the dependent parts and extends in the shape of some irregular patches to the anterior thoracic regions. Some foamy, slightly blood-tinged fluid escapes from the anterior nares. No

<sup>1</sup> We believe the reason for the rapid change of the eosin-methylene-blue to be the following: It is impossible completely to dehydrate sections in an atmosphere saturated with moisture. Hence, after a time the water in the sections will dissolve some eosin, and the eosin solution so formed will in its turn dissolve the methylene-blue. Whether this explanation be correct or not, it does not alter the fact continually observed, that sections stained with eosin and methylene-blue during the rainy season in Manila rapidly fade and, to a great extent, become useless for the study of finer structural details and the presence and distribution of the bacteria.

wounds or ulcerations or abrasions are found anywhere on the surface. The left inguinal region presents a swollen area about 6 to 8 centimeters long and 5 to 6 centimeters wide, which is quite hard, somewhat elastic, and nonfluctuating. No individual glands or groups of glands can be mapped out in the swollen area. The skin is here adherent to the underlying tissues. The hard infiltrated area extends upwards into the inguinal canal. Dark fluid blood escapes from the veins upon section of the body. The serous membranes are injected and dull, and all serous cavities contain a somewhat increased amount of slightly turbid fluid. The increase is most marked in the abdominal cavity. The pericardium is smooth and otherwise normal, except as to the presence of a number of small punctiform subepicardial hemorrhages, which are dotted all over the external surface of the heart. All diameters of the heart are about one and one-third of the normal measurements. The wall of the left ventricle shows considerable hypertrophy. The left auriculo-ventricular opening is normal in diameter, the right one easily admitting four fingers. The myocardium is quite soft and flabby, and pale pinkish-yellow in color. Otherwise the heart is normal. The coronary vessels and their branches are much congested. The lungs are normal in shape and moderately inflated. The upper lobes are pinkish-gray, the lower purplish-blue in color. The latter much congested and quite œdematous. The mucosa of the bronchi, the trachea, and the larynx is swollen and reddened and the veins injected. The epiglottis is much injected, and the papillæ circumvallatæ of the tongue swollen. The spleen is enlarged to two to three times its average size; it is somewhat softer than usual. The capsule is smooth and grayish-blue in color. On section it is brownish-red. The pulp does not protrude, the cut surface is smooth, and the trabeculæ and follicles are distinct. The kidneys are normal in size, the capsules smooth and grayish-yellow with some purplish-gray. The capsule peels off easily. On section the blood vessels are found to be injected, the tubules light yellow, and the surface as a whole dull. The Malpighian bodies are not distinguishable. The mucosa of the bladder shows a very few small, submucous, punctiform hemorrhages. The prostate, etc., are normal. The adrenals are soft, swollen and brownish-yellow. The serosa of the stomach is much injected, the mucosa in an intensely hemorrhagic condition. Small hemorrhagic spots are found all over the mucosa on the anterior

wall. Midway between the larger and the lesser curvature a number of hemorrhagic spots have become confluent. The hemorrhagic spots can not be wiped off. The lower part of the esophageal mucosa is likewise much congested. The serosa of both the small and the large intestine is congested and dull. The mucosa shows hemorrhagic spots, particularly in the duodenum. The follicles are swollen. Several *Ascaris lumbricoides* were found in the esophagus. The capsule of the liver is smooth and transparent, the external color is ochre-yellow, the cut surface is fairly smooth and yellow to light brown. The lobules are not enlarged; the connective tissue does not appear increased. The veins contain much blood. The organ, as a whole, is small and peculiarly formed; the left lobe forms merely a small appendix to the right one. The weight is 1,210 grams. The length of the longest transverse diameter is 20 centimeters, the sagittal diameter (antero-posteriorly) 9 centimeters, the thickness from above downwards is 12 centimeters. The left lobe measures 3 centimeters from side to side, 9 centimeters from before backwards, and is 2 centimeters thick. When an incision is made over the left inguinal bubo, it is found that the skin is completely adherent to the subcutaneous tissue, fascia, etc. There first escapes quite a quantity of yellow, blood-tinged serum, and the tissue beneath the skin presents a condition of complete hemorrhagic infiltration. The glands have become confluent, their capsules, except that of one, being indistinguishable from one another. The hemorrhagic infiltration and the œdema extend into the inguinal canal. In the left half of the pelvis the tissues are very œdematous, the loose areolar tissue is yellowish and almost gelatinous; and imbedded in this tissue are swollen, softened, hemorrhagic lymph glands. The iliac glands are in the same condition; the retroperitoneal glands at the bifurcation of the aorta into the common iliac arteries, and even the ones farther up along the abdominal aorta, likewise present a similar appearance.

Smears made from the inguinal glands and from the spleen show very numerous plague bacilli. The organisms are most abundant in the glands.

*Anatomical diagnosis.*—Hypertrophy of the heart; congestion and fatty degeneration of the kidneys; fatty infiltration and degeneration of the liver; hemorrhagic inflammation and hypertrophy of the left inguinal, femoral, iliac, and retroperitoneal glands; hypertrophy, softening, and congestion of the lymph glands

in general; multiple subserous and submucous hemorrhages. Bubonic plague.

Culture tubes inoculated from the inguinal glands developed a typical plague growth.

*Microscopic examination.*—Glands: The inguinal glands, the iliac, and the retroperitoneal, all practically show the same changes, which, however, are more profound in the lowermost lymph nodes. All glands contain large tracts of tissue in an advanced state of coagulation necrosis; there is much blood extravasation, which extends into the periglandular loose areolar tissue. The latter also shows much infiltration with leucocytic elements. The capsules of the glands are completely loosened by the same type of infiltration. The blood vessels are dilated and engorged, and their walls show hyaline swelling and inflammatory loosening ("Auflockerung"). Weigert's method shows both solid and tubular wall thrombi in many of the vessels of the gland substance proper, in the capsule, and in the periglandular areolar tissue. Much fibrin is also found in the shape of reticular deposits throughout the sections. In some places a continuation of an intravascular thrombus into an extraglandular network is visible. Plague bacilli, freely scattered throughout the sections, are found either in large masses, in small groups, or as single individuals.

In the spleen the follicles are sharp in outline and the boundaries of the pulp spaces indistinguishable. The latter are densely crowded with cellular elements among which the erythrocytes much predominate. Besides the common small mononuclears and eosinophilics, a fair number of large mononuclears with hyaline protoplasm, which stains moderately with methylene blue, are found. Plague bacilli are seen all throughout the sections; however, nowhere are they present in large groups, but thinly scattered here and there. A few threads of fibrin are occasionally seen.

Kidneys: The renal tissue exhibits complete degeneration of the tubular epithelium, with cloudy swelling and fatty degeneration. The degeneration is most marked in the convoluted tubules, while in the straight tubules apparently normal epithelia are found here and there. The uriniferous canaliculi contain a great deal of granular material. The glomeruli show much dilated capillaries; otherwise they present no marked changes. The renal vessels are all much congested. The interstitial connective tissue is quite œdematous.

In the liver we find small interlobular inflammatory foci, composed of small, round cells. The parenchyma cells are finely vacuolated or coarsely granular; some of the nuclei are absent or do not stain. Here and there a small area is found in which all cells are degenerated (areas of focal necrosis). A few plague bacilli are here and there seen in the capillaries, but none in the interlobular inflammatory foci.

The consolidated areas of the lower lobes of the lungs show an enormous dilatation and engorgement of the vessels and alveoli, completely filled with extravasated blood and with desquamated alveolar epithelial cells. The latter contain much dark granular pigmentary matter. Here and there one sees in the alveoli, cocci, a slender bacillus, and possibly a few plague bacilli. Whether the latter are really plague bacilli is somewhat doubtful; certainly, if present at all, they are very scantily represented.

#### CASE No. 2. LEFT INGUINAL BUBO.

[Necropsy Protocol No. 989. T. C., a male Chinese, from Ilang-Ilang Street, San Nicolas, 29 years of age. Ill two days. Died June 20, 1904. Post-mortem examination nine hours after death.]

The body of a slender, rather poorly nourished Chinese. Post-mortem rigidity is still well-marked. Post-mortem lividity is extensive. The anterior abdominal wall presents a mottling of greenish discoloration. The tibial region of the left leg shows two shallow, almost healed ulcers. Both the inguinal regions are swollen, particularly the left one. The swelling shades off into the surrounding tissues. On the right side no individual glands can be distinguished, because the whole region is much infiltrated and edematous. On making an incision into this region, a considerable amount of slightly blood-tinged, serous liquid escapes and the entire tissues are found to be diffusely infiltrated with blood. The individual glands can not be distinguished, as they have become fused into one irregular hemorrhagic mass; nor are the capsules, the cortices, or the medullæ of the individual glands distinguishable. No suppurative changes are observed. On the right side the glands are swollen, softened, and highly congested. However, the capsules are well preserved, and the hemorrhagic condition does not extend beyond the glands proper. The other superficial glands are not palpable. On opening the body cavities, a moderate amount of dark, fluid blood escapes from the veins.

The abdominal cavity contains an increased amount of serous,

blood-tinged fluid. The hemorrhagic infiltration of the inguinal region extends through the inguinal canal, into the pelvis, and along the iliac vessels and left ureter upwards. The pericardium contains a normal amount of serous fluid, but it is blood-stained, evidently by post-mortem imbibition. The heart presents a few small subepicardial hemorrhagic areas. The myocardium is soft and flabby, and pink in color.

The beginning of the aorta presents an atheromatous ulcer, surrounded by a calcareous deposit. Otherwise the heart and the great vessels are normal. The pleural cavities contain a moderate amount of blood-tinged fluid. The pleural surfaces of the lungs are dark purple, with some greenish putrefactive areas. The lungs are full of blood and contain but little air. The bronchi, the trachea and, to a lesser extent, the larynx show a congested mucosa. The spleen is enlarged to about twice its normal size. It is steel-gray-purplish on the external surface, and brownish-red on section. The pulp is soft. The Malpighian bodies are fairly distinct. The kidneys are normal in size, purplish-blue in color. On section they are dull and decidedly grayish yellow. They are exceedingly soft, a condition probably due to some extent, at least, to post-mortem changes. The mucosa of the left ureter is highly congested and shows some hemorrhagic spots, that of the right ureter is congested, but to a much lesser extent. The mucosa of the bladder shows a minor degree of congestion. The liver is normal in size, rather increased in consistency, and dark purplish in color with some grayish-yellow mottlings. It cuts with increased resistance, and the cut surface is yellow brown in color. The liver lobules are increased in size. The gall bladder and its ducts are normal. The duodenum and the stomach show a highly congested mucosa. The gastric mucous membrane exhibits numerous small punctate or somewhat larger, irregular hemorrhagic spots. The follicles of both the small and the large intestine are highly swollen and congested. The suprarenals are swollen, soft, and dark yellowish-brown in color. The pancreas is normal. The abdominal glands in general are all more or less swollen, congested, and softened.

*Anatomic diagnosis.*—Hemorrhagic left inguinal bubo; general lymphadenitis; multiple hemorrhages into the serous and mucous membranes; congestion and parenchymatous degeneration of the kidneys; congestion and fatty degeneration of the liver; bubonic plague.

A microscopic examination of smears from the left inguinal glands shows innumerable plague bacilli, most of which are oval, or almost spherical, in form, with a narrow peripheral stained margin, suggesting mere empty shells. Smears from the right inguinal glands contain a moderate number of plague bacilli, which are also quite numerous in the juice of the spleen. The heart's blood contains several varieties of micro-organisms in moderate numbers. Among them possibly a very few plague bacilli are present.

Tubes inoculated from the left inguinal bubo and from the spleen developed a typical plague growth.

*Microscopic examination.*—Left inguinal glands: The finer gland structure is practically completely lost, though follicles can here and there still be recognized to some extent. All of the vessels show great dilatation and engorgement, and the connective tissue at the hilum is increased; toward the periphery tracts of coagulation necroses are seen. Here the œdema is also marked. All throughout the glands there are found masses composed of innumerable, very densely crowded plague bacilli. In sections stained with eosin-methylene-blue, but which have been too much decolorized, the bacillar masses are somewhat stained by eosin and they look simply like ordinary granular material, for which in such improperly stained sections they may easily be mistaken. It is particularly the periphery of the gland which is quite extensively infiltrated with red blood corpuscles. This extravasation extends beyond the capsule and into the surrounding loose areolar connective tissue, where it is mixed with a more or less marked leucocytic infiltration. The parenchyma cells of the glands are small mononuclears and some plasma cells, polynuclears of the ordinary type, and a few eosinophilics. In sections stained by Weigert's method, numerous capillaries and other small vessels are found to be closed by hyaline fibrin thrombi. This thrombosis is generally complete in the smallest vessels only. In the larger ones we see an incomplete thrombosis. The fibrin in the latter is deposited on the intima and leaves a free space in the center of the vessel, which, however, may show an open network of fibrin filaments. The endothelial lining of the vessels, totally or partly thrombosed, is apparently generally intact, although there may be seen places where the endothelia are missing. Such losses are probably due to an artefact. The vessel walls proper do not show any profound changes; however, a minor



degree of œdema and even of hyaline degeneration may here and there be observed. No bacilli are seen in the lumina of the vessels, either in those containing thrombi or in those free from them. In the right inguinal glands the most pronounced pathologic change is the increase of connective tissue at the hilum and the great dilatation and engorgement of the vessels. The congestion is greater on the right side than on the left. This is to be attributed to the fact that there are only few bacilli present on the former one, while on the latter they are so numerous as to have a tendency more or less to crowd all of the autochthonous tissue elements. Some few of the vessels in the right inguinal glands show a network of fibrin, however, none complete thrombosis.

The spleen sections show very numerous plague bacilli. However, they are nowhere found in dense masses as in the primary bubo, but very abundantly as single individuals freely distributed between the cells. The boundaries of the follicles are rather indistinct. The pulp spaces contain numerous crowded red blood corpuscles. In a few small vessels tubular hyaline thrombi are seen.

The epithelial lining of the uriniferous tubules of the kidneys shows cloudy swelling and fatty degeneration. These changes are most marked in the convoluted tubules, but the epithelia of the straight ones are likewise much affected. Much granular material is found in all of the tubules. The intertubular connective tissue is œdematous. In a number of the glomeruli the capillaries are closed by hyaline fibrin thrombi, while other capillaries are free and non occluded. The thrombi mostly are solid, though some are distinctly tubular with an open lumen in the center. Occasionally one sees a thrombus extending from a Malpighian tuft into an afferent or efferent, or intertubular vessel. Changes of the vascular endothelium of the thrombosed vessels are not demonstrable. All through the renal (and also through the hepatic) tissue, fairly numerous large bacilli, which retain Gram's stain, are found. These micro-organisms clearly represent a post-mortem invasion found frequently in Manila in bodies, when the post-mortem examination can not be made immediately but has to be postponed for some time. Plague bacilli are not seen in the renal tissue.

In the liver the parenchyma cells are finely vacuolated; large, coarse vacuoles are not seen. The capillaries are dilated, par-

ticularly those in the central part of the lobules. Here and there a small, interlobular, inflammatory focus, composed of mononuclears, is found. The interlobular fibrous connective tissue is somewhat increased; otherwise marked changes are not seen.

In the lungs the capillaries and the veins are much engorged. The alveolar spaces contain much granular detritus, many desquamated endothelial cells and considerable numbers of large bacilli taking Gram's stain. These organisms are also found in large numbers in the liver and the kidneys. No plague bacilli are encountered in the sections.

### CASE NO. 3. LEFT INGUINAL BUBO.

[Necropsy Protocol No. 940. S. Y. S., male Chinese, 25 years old, from 70 Santo Cristo, Binondo. Ill six days. Died April 14, 1904, at 5.30 o'clock a. m. Post-mortem examination six hours after death.]

The body of a male Chinese, about 35 to 45<sup>1</sup> years old. Well-developed muscles and skeleton. Rigor mortis well marked. Post-mortem lividity of a dark port-wine red color is present over the dependent parts of the body, also around the neck, on the sides of the trunk, and over the anterior tibial regions. The integument in general is quite cyanotic. On the left leg over the sharp edges of the tibia, midway between the ankle and the knee, are seen three small oval ulcerations; they have the size of a split pea and are covered with a dry, dark brown crust. Below these shallow ulcers are about a dozen depressed, healed cicatrices of the same size as the ulcerations. The lymph glands below the left ligament of Poupart are swollen and the skin here is covered with tenacious brown ointment. After its removal the integument is found unbroken, but puffed up and œdematous. The round swelling which protrudes over the surrounding skin has the size of a walnut, feels doughy, and is rather firm; but the individual glands are not distinctly palpable. On section of the skin there escapes first a small amount of yellowish, watery fluid, which becomes bloody as soon as the subcutaneous adipose tissue is cut into. The glands of this region have become fused together, and the individual components of the group are indistinguishable. The whole tissue shows an intense hemorrhagic infiltration and well-marked softening. A good deal of dark, bloody fluid can be scraped off from the cut surface and it can be seen that the hemorrhagic infiltration

<sup>1</sup> The deceased was evidently much older than the figure given officially in the death certificate.

extends beyond the glands into the periglandular and general subcutaneous connective tissue. The capsules of the glands are indistinguishable.

After opening the abdomen, the left iliac glands are found in the same condition as those in Scarpas' triangle. They form a bubo of the size of a small walnut. However, those higher up are much less affected; they are moderately increased in size and dark purple in color, but there is no marked hemorrhagic infiltration beyond the gland substance. The peritoneum, the pleura, and the pericardium show deeply injected, dilated vessels. The intestinal serosa appears dull and exhibits slight greenish discoloration; shining through it are found hemorrhagic spots in moderate numbers both in the small and in the large intestine. The pericardium contains a normal amount of clear straw-colored fluid. The epicardium shows greatly congested vessels and a number of flat, slightly elevated, yellowish-gray, old, fibrous cicatricial bands. These are found on the right side, over the auricle and the ventricle. The auriculo-ventricular zone exhibits quite a number of small petechiæ from the size of a pin head to that of a millet seed. The right ventricle is much distended and contains a large amount of dark red, fluid blood; the left ventricle is firmly contracted and contains a small, dark red, firm clot. The heart as a whole is moderately hypertrophied, the walls of the left ventricle are thickened, and those of the right rather thin and flabby. The myocardium in general is firm, and on section of a dull, brownish-pink color. The arch of the aorta shows a number of atheromatous patches. Both lungs are quite heavy, their upper lobes being of a slate-grayish-pink color and the lower ones dark bluish-purple. On the cut surface the upper lobes are moist and their vessels discharge a moderate amount of dark blood; the lower ones are brownish-red and their tissues are very rich in dark, fluid blood and very poor in air. The small bronchi of the lower lobes contain a bloody, foamy, fluid; slightly blood-tinged, foamy, viscous fluid is also found in the trachea. The mucosa of the bronchial tree, of the trachea, and of the larynx is slightly swollen and much injected. The bronchial glands are not enlarged; however, they are very dark in color and much congested. The spleen is much enlarged, its diameters being 24 by 12 by 5 centimeters. All the hilus vessels are much enlarged. The capsule is smooth and transparent everywhere, except in one place at the

upper convex surface, where it is somewhat thickened, though not elevated, and opaque and dull grayish-white in appearance. The cut surface of the organ is dark brownish-red; the trabeculae can be seen very well and are distinctly thickened; the pulp is moderately soft; and a moderate amount of juice can be scraped off the cut surface. The Malpighian corpuscles are not distinguishable. On the whole the consistency of the spleen is rather increased than decreased. Its weight is 675 grams. The kidneys are normal in size, much congested, and the capsules are rather dull and not very translucent. The outer surface is dark purplish-blue. Here and there a grayish-white mottling is seen. The capsules peel off easily. On the cut surface the vessels appear injected, the tubules decidedly grayish-yellow. The glomeruli are not very distinct, and the pyramids are dark pinkish-purple in appearance. The relation of the cortex to the medulla is normal. The mucosa of the pelvis is smooth and much injected, so that the small vessels are distinctly visible. The suprarenals are normal in size, moderately injected, yellowish-brown in color, and somewhat softened. The liver is of normal size, the capsule very tense, shining, and transparent. The external color is bluish-purple. The cut surface discharges a rather moderate amount of dark, fluid blood. The liver lobules are distinct and of a dark brownish-yellow color. The gall bladder is distended with very dark, turbid, pitchy bile. The mucous membrane is swollen. There are no stones. The ducts are normal. The serosa of the stomach and intestines is injected, that of the latter being of a dull appearance, as before described. The dark spots seen through the intestinal serosa correspond to hemorrhagic spots of the mucosa. The gastric mucosa shows numerous small, punctiform petechiae on a dirty grayish background. The pancreas, the prostate, and the bladder show no particular changes.

*Anatomic diagnosis.*—Hypertrophy and hemorrhagic inflammation of the left inguinal and iliac glands; passive congestion and parenchymatous degeneration of the kidneys; congestion and cedema of the lungs; multiple subserous and submucous hemorrhages; moderate hypertrophy of the heart; old epicardial cicatrices; atheroma of the aorta; splenomegaly. Bubonic plague.

Smears made from various organs show the following: From the primary bubo, quite a number of very poorly staining oval or round bacilli. Only a very small peripheral rim has taken the dye; the center is entirely unstained. These bacilli appear as empty shells.

Another bacterium present is a long, slender, well-stained bacillus. The juice from the spleen contains a moderate number of plague bacilli; that from the liver and the kidneys a few only; none at all are found in the smear from the heart's blood. Cultures inoculated from the inguinal glands and from the spleen developed plague bacilli; a tube from the liver remained sterile.

*Microscopic examination.*—The glands of the inguinal region show a marked increase of connective tissue and thickening of the walls of the vessels at the hilum. While some portions still exhibit a fairly normal lymphoid tissue others are thoroughly infiltrated with extravasated blood. The loose, areolar, pericapsular connective tissue is infiltrated with mononuclear and polynuclear inflammatory cells. Innumerable plague bacilli are diffused throughout the gland and penetrate into the periglandular connective tissue. Here and there a moderate amount of fibrin is seen, particularly around some small vessels, but hyaline thrombi obliterating the vascular lumina are not visible. The capsule of the spleen is not thickened, but the trabeculae are broad. The Malpighian bodies are quite small, not sharply defined, and shade off gradually into the surrounding tissue. The fibrillar connective tissue of these follicles is increased. The pulp spaces are fairly well recognizable and are densely filled with red blood corpuscles, while a moderate number of polynuclears, some typical plasma cells, and large mononuclear cells are also present. The last, which appear to be proliferated endothelia of the pulp spaces, have a large vesicular round or oval nucleus, not very rich in chromatin, with generally one or more distinct nucleoli. A moderate number of plague bacilli is found in the spleen sections. The kidneys show both large and small vessels to be greatly engorged. There is extensive cloudy swelling of the epithelium of the uriniferous tubules, and a moderate amount of granular material is scattered through the latter. The liver exhibits engorged capillaries and a very moderate degree of fatty degeneration of parenchyma cells. Very small interlobular inflammatory foci are seen in a few places. The pulmonary tissue shows an enormous engorgement of the blood vessels. Most of the alveoli are open and empty, but a moderate number contain red blood corpuscles, or more or less granular material, in which are embedded leucocytes and shreds of fibrin, the latter forming a network like that occurring in fibrinous pneumonia. Plague bacilli are not found in such small

incomplete areas of consolidation. The stomach shows engorgement of the veins of the submucosa. The congestion is continued into the small veins and capillaries of the mucosa. Blood is found extravasated between the glands and upon the surface of the latter. The cells lining the peptic glands show evidence of nutritive disturbance. Here and there one sees karyokinetic figures, while a number of the sustentacular central cells show two or more nuclei. Plague bacilli are not seen in the mucosa.

#### CASE NO. 4. RIGHT INGUINAL BUBO.

[Necropsy Protocol No. 932. F. H., young male Filipino, from 20 Alma Street, Tondo. Died March 20, 1904, at 2 o'clock p. m. Post-mortem examination made March 21, at 10 o'clock a. m., twenty hours after death.]

Body of an unusually strong young native, of 20 to 25 years of age. The right heel shows a large, open, ulcerated surface about the size of the palm of the hand, dark purplish in color, covered with a dirty greenish fibro-purulent secretion. The entire anterior surface of both legs shows a scaly vesicular eruption. Post-mortem lividity is well marked all over the body. The skin in general is markedly cyanotic. Post-mortem rigidity has almost disappeared. Putrefaction is well advanced.

On opening the abdomen a great deal of ill-smelling gas escapes. The superficial blood vessels discharge a moderate amount of dark, fluid blood. The serous membranes are quite dull, their vessels are markedly injected. Heart: The left ventricle is well contracted, the right ventricle dilated. The visceral pericardium is strongly injected and shows a few small hemorrhagic areas. The myocardium is pinkish in color, and fairly firm in consistency. Valves normal. Endocardium smooth. The large vessels are normal. Lungs: Slightly adherent to the pleura costalis. Extensively adherent to the upper surface of the diaphragm. The upper lobes are pinkish in color and contain a good deal of air; the lower lobes are highly congested and of a dark purplish color; they contain but little air, are very œdematous and full of dark fluid blood. The mucous membrane of the bronchi and of the trachea is swollen and congested; the air tubes contain a moderate amount of frothy, viscid mucus. Larynx likewise congested. Spleen: Normal in size; the capsule is smooth and slightly wrinkled and the outer surface is dark purple in color. The cut surface is dark brown, the pulp is soft. A good deal of dark-brown juice can be scraped off the surface. The Malpighian bodies are not distinctly visible.

The trabeculae are fairly well marked. Kidneys: Capsules smooth, surface purplish in color. After removal of the capsules, which peel off easily, the glomeruli stand out as highly injected points, surrounded by a grayish white tissue. On section the glomeruli, the vessels, and the pyramids appear highly congested. The tubules are grayish white. The pelves are smooth and much congested. The surparenals are enlarged, soft, oedematous, and congested. Brownish purple in color. Liver: The liver is somewhat swollen, capsules smooth and transparent. Outer surface purplish gray. The cut surface is purplish brown. The vessels discharge a good deal of fluid blood. Boundaries of liver lobules distinct. The gall bladder is of a dark grayish purple color. Its mucous membrane is swollen and congested. The viscus contains a large amount of dark greenish turbid bile. No stones. Stomach and intestines: The serosa is rather dull, showing injected vessels. A number of small hemorrhagic spots are seen on the serosa of the small intestines. The mucous membrane of the stomach is grayish-white and shows a number of small hemorrhagic spots. It is covered with dirty gray, tenacious mucus. The small intestine likewise shows some small hemorrhagic spots in its mucosa. Lymph glands: The inguinal glands of both sides are much swollen, rather soft, oedematous, congested, and purplish in color. These changes are more marked on the right side than on the left. The mesenteric lymph glands show similar changes, though to a less degree. The cervical glands show only a very moderate amount of enlargement and congestion.

*Anatomical diagnosis.*—Large granulating ulcer on the right heel. Congestion and oedema of the lungs. Passive congestion of the liver and kidneys. Parenthymatous degeneration of the kidneys. Oedema, general hypertrophy, and congestion of the lymph nodes, particularly of those of the right inguinal region. Multiple subserous and submucous hemorrhages. Bubonic plague.

Smears are made from the heart's blood, spleen, liver, and left inguinal glands. The smears from the heart's blood show only a few pest bacilli, while those from the spleen and glands show a considerable number. Culture tubes are inoculated from the heart's blood, spleen, and liver. The tube from the spleen developed a pure culture of plague bacilli; those from the liver and the heart's blood showed a mixed culture of plague bacilli and staphylococcus pyogenes albus.

*Microscopic examination.*—The inguinal lymph glands show an oedematous infiltration and great dilatation and congestion of blood vessels. The perivascular connective tissue at the hilum is much increased. An area of extensive blood extravasation is found near the capsule. The majority of the parenchyma cells of the gland are small mononuclear and ordinary polynuclear cells; plasma cells are fairly numerous, and plasma mast cells are plentiful. Here and there are seen globular, homogeneous masses of a diameter of 20 to 30  $\mu$  and more which have a strong affinity for eosin. Neither the blood vessels nor the other parts of the tissues show any fibrin. Plague bacilli are only sparingly seen in sections of the glands. Sections of splenic tissue show mostly ill-defined Malpighian corpuscles, obliterated pulp spaces, and an overcrowding of the latter with red blood corpuscles. As in the lymph gland tissue, plasma cells and plasma mast cells are numerous. Bacilli are found in small numbers only. The renal tissue shows greatly dilated and engorged vessels, very small areas of blood extravasation between the tubules, an occasional thickening of Bowman's capsule, and most extensive cloudy swelling of the tubular epithelium. While the latter is still found intact here and there, most tubules, both convoluted and straight, are lined by greatly swollen, irregular, hazy cells in which a nucleus is not seen, or if seen at all, it is very poorly stained.

In the pulmonary tissue one sees enormously engorged interalveolar capillaries and air spaces partly filled with desquamated-epithelia and erythrocytes. No fibrin is found in the alveoli.

#### CASE NO. 5. RIGHT INGUINAL BUBO.

[Necropsy Protocol No. 977. O. C., Chinese, 25 years, male, from 214 San Jacinto Street. Died after an illness of two days on May 25, 1904, 9.15 p. m. Post-mortem examination fifteen hours after death.]

Body of a young male Chinese about 25 years old; rather slender, but well developed. Post-mortem rigidity moderately well marked. The skin as a whole is quite cyanotic, and the post-mortem lividity, which has extended well to the anterior surfaces, is marked. A small amount of dirty-brown foamy fluid exudes from the nares. No wounds or ulcerations are to be found anywhere on the integument. The right inguinal region is somewhat swollen, but the swelling is not high; it is not well defined but shades off gradually into the surrounding tissue. The swollen area is markedly cyanotic and cedematous, the skin here pits on pressure. On section the



subcutaneous connective tissue discharges a serous, slightly yellowish fluid, and on further dissecting into the tissues an extensive hemorrhagic infiltration is encountered. This hemorrhagic infiltration surrounds ill-defined, swollen, soft, and hemorrhagic glands. The bloody extravasation extends from Scarpa's triangle through the inguinal canal, into the pelvis along the iliac glands, thence into the abdominal cavity up to the region of the kidney. All lymph glands along this course are swollen, much softened, and hemorrhagic. The same pathologic changes, though to a lesser degree, are shown by the mesenteric, the peritoneal, the mediastinal, and the bronchial glands. The latter are more markedly enlarged, softened, and hemorrhagic than any other glands mentioned except those of the chain beginning with the right inguinal glands. The superficial lymph glands, aside from the right inguinal, are moderately swollen, softened, and congested. Subserous hemorrhagic spots are found on the epicardium, on the pleuræ, on the external surfaces of the stomach, the small intestines, the kidneys, and on the capsule of the liver at the insertion of the suspensory ligament. The pericardium is smooth, much injected, and contains a moderate amount of fluid. The heart shows a number of subepicardial hemorrhages, varying in size from a small point to irregular spots several millimeters in diameter. These petechiæ and ecchymoses are found on both ventricular surfaces and on the sulcus. The myocardium is of fair consistency. No further dissection of the heart is made, since it is to be preserved as a museum specimen. The lungs are well expanded, their pleuræ smooth, nonadherent, and dark purplish-blue, with a moderate number of small hemorrhagic spots and with some small elevated emphysematous areas on the lower lobes. On section the pulmonary tissue is of dark purplish-brown color, containing very much dark blood and foamy, aqueous fluid. The lungs on the whole are heavy and contain but little air. The bronchial, tracheal, and laryngeal mucosa is somewhat swollen and greatly congested. The epiglottis is of a dark purplish-blue color. The spleen is normal in size, the capsule slightly wrinkled, transparent, and bluish-gray. The organ as a whole is fairly firm. The cut surface is reddish-brown and granular. The amount of juice which can be scraped off the surface is quite moderate. The trabeculæ and corpuscles are distinct.<sup>1</sup> The kidneys

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<sup>1</sup> Many plague bacilli were found in the smears from the spleen; yet it was neither enlarged nor softened.

are much congested and very soft. Externally they are dark bluish-gray, with some subcapsular petechiæ and ecchymoses. On section the vessels are greatly engorged, the tubules grayish-white, and the surface as a whole dull. The mucosa of the pelvis and bladder is greatly congested. The mucosa of the ureters and the bladder is moderately congested, but shows no hemorrhages. The suprarenals are large, swollen, soft, and dark yellowish-brown. The liver is large, its margins rounded, its capsule thin and transparent, and its external color a yellowish-bluish-purple, alternating with decidedly grayish-yellow areas. Along the insertion of the suspensory ligament are seen numerous subcapsular hemorrhages, varying in size from a mere point to a diameter of 5 to 7 millimeters. The organ is of much increased consistency, and the cut surface is brownish-yellow in color. The gall bladder is distended with dark yellowish-green bile. The serosa of the stomach and intestines shows a number of hemorrhagic spots. The gastric mucosa is studded with small hemorrhagic areas and so is that of the duodenum, though to a lesser extent. The lymph follicles of the intestines are swollen.

*Anatomic diagnosis*—Congestion of the lungs; congestion and parenchymatous degeneration of the kidneys; fatty degeneration of the liver; multiple subserous and submucous hemorrhages; multiple hemorrhagic lymphadenitis. Bubonic plague.

Smears from the right inguinal glands show innumerable typical plague bacilli; those from the spleen show numerous pest organisms. Culture tubes inoculated from the inguinal glands and the spleen developed a typical growth.

*Microscopic examination*.—The inguinal glands show an enormous dilatation and engorgement of the blood vessels, a moderate degree of free blood extravasation, and marked œdema. A number of the smaller blood vessels are completely obliterated by hyaline thrombi. Other larger vessels show closely packed blood corpuscles and a network of fibrin between the corpuscles. The number of leucocytes in the engorged blood vessels, including those which show a network of fibrin, is very moderate. If at all increased over the normal, they are not very greatly so. Any damage to the vessel walls, which are much dilated, is not demonstrable, and the vascular endothelium appears intact. The cellular elements of the gland are the same as in the other cases described above. Plague bacilli are very numerous. However, they do not form dense, almost solid masses, but infiltrate the intercellular spaces

and surround, as it were, each individual cell. Spleen: The boundaries of some of the Malpighian corpuscles are distinct and sharply cut; others show an indistinct limitation, because the small mononuclear cells forming the follicles are densely infiltrating the neighboring tissues. The pulp spaces are quite indistinct, because they are crowded with cells. Most of these are leucocytes, but in some places red blood corpuscles predominate. All through the pulp spaces of the splenic tissue a fibrin network can be seen. No fibrin, however, is found in the vessels and the network has, of course, no intravascular connection. Here and there one can see the fibrin threads take their origin from leucocytes. Plague bacilli are present in large numbers. Kidneys: The glomeruli do not show any marked changes, but the capillaries of the tufts are greatly engorged with blood. In general all renal vessels, particularly the capillaries and the smaller veins, are much engorged. In a few places, near the capsule, small areas of blood extravasation are encountered; however, none are found at a distance from the surface. The epithelium of the convoluted tubules shows considerable cloudy swelling and also more profound degeneration, with complete loss of nuclei. The tubular lumina are generally filled with more or less granular detritus. Few, and not greatly advanced, changes are seen in the straight tubules. No bacilli are seen in sections from the kidneys. All parenchyma cells of the liver are in an advanced stage of fatty degeneration and their nuclei are either poorly or not at all stained. Aside from this degeneration the hepatic tissue shows no marked changes. Sections from the lungs present greatly engorged capillaries; the alveoli are partly filled with desquamated epithelia, red blood corpuscles, and a granular detritus. Plague bacilli are not found. In the gastric mucosa the interglandular capillaries are much enlarged and free blood is found between the glands up to the very uppermost strata. However, no blood is seen on the free surface of the mucosa.

#### CASE No. 6. RIGHT INGUINAL BUBO.

[Necropsy Protocol No. 998. Post-mortem examination performed on July 3, 1904, twelve to eighteen hours after death, upon the body of V. D., from 17 Azcarraga Street, Tondo; a male Filipino 17 years old.]

Post-mortem rigidity is not well marked; it has evidently begun to disappear. Post-mortem lividity is noticeable over dependent parts of the body. The integument, particularly around the chest, the neck, and the face is quite cyanotic. The right inguinal glands,

particularly the lowermost ones, show considerable swelling. The latter are enlarged to the size of a walnut. The skin is unbroken. The region is quite firm and hard, somewhat œdematous, but not fluctuating. The boundaries of the individual glands can not be well differentiated and the swelling shades off gradually into the surrounding tissues. A chain of swollen indurated glands can be felt along the spermatic canal. On opening the body, the abdominal cavity shows a moderate amount of slightly turbid fluid. The serosa is dull. The intestinal serosa is deeply injected, and here and there small hemorrhagic spots are seen. The general color of the intestinal serosa is varied by some greenish discoloration due to putrefactive changes. On the right side all the iliac glands are swollen, much congested, and more or less hemorrhagic on section. In fact, the whole chain of glands from those in Scarpas' triangle up to the retroperitoneal ones, and as far as the kidneys, is in this condition. The hemorrhagic infiltration is most marked in the inguinal glands. There it extends into the periglandular connective tissue, the individual glands have become confluent, and their capsules and their finer structure have become indistinct. The heart shows a larger number of irregular subepicardial hemorrhages, measuring from 1 to 5 millimeters in diameter. They are situated over the left ventricle. The myocardium is fairly firm, pinkish, with a slightly yellowish tint. Otherwise normal. The lungs are very slightly adherent by some few thin adhesions. The upper lobes contain a fair amount of air and are pinkish-purple in color. The lower lobes are heavy, congested, œdematous, and purplish-blue in color. A few subpleural hemorrhagic spots are seen on the lower lobes. Bronchi, trachea, larynx show an injected mucosa. The papilæ circumvallatæ of the tongue are much swollen. The spleen is 15 by 12.5 by 6 centimeters. It weighs 645 grams. Capsules smooth, transparent, steel-grayish-blue; consistency fairly firm. Cut surface brownish red. Malpighian bodies not very distinct, trabeculæ distinct; cut surface slightly granular, amount of juice which can be scraped off, moderate. Kidneys normal in size, soft; capsules smooth, peel off easily. Pinkish purple showing a few small subcapsular hemorrhages. Cut surface, vessels injected, tubules yellowish gray, dull. Pelves smooth. The lower third of the left ureter is dilated to three times its normal diameter. The bladder contains several ounces of turbid urine. On the right side posteriorly below the apex, there is seen a flat elevation about

the size of a split bean. There the tissue is purplish-pink and the swelling appears somewhat like an enlarged lymph gland. On section this part seems somewhat tubercular, and one of the nodules projects into the vesical mucosa. Otherwise the mucosa is smooth, moderately congested. Prostate normal. Suprarenals swollen, soft, yellowish-brown. Liver rather small. Capsule smooth, transparent, much grayish-yellow mottling alternating with a pinkish-purple. On section, veins moderately filled, cut surface slightly granular, boundaries of acini distinct; color ocher-light brown. Gall bladder normal. Gastric duodenal and general intestinal serosa and mucosa injected. Lymph follicles of small and large intestines somewhat swollen. Mesenteric, retroperitoneal, and other lymph glands swollen and congested.

*Anatomical diagnosis.*—Congestion of the lungs; congestion and parenchymatous degeneration of the kidneys, splenomegaly, interstitial hepatitis with fatty degeneration, hemorrhagic lymphadenitis of the right inguinal glands. General hypertrophy and congestion of lymph glands. Subserous and submucous hemorrhages. Bubonic plague.

Smears from the right inguinal glands show numerous, those from the spleen a moderate number of plague bacilli. No Donovan-Leishman bodies found in the splenic juice. The liver smears exhibit a very few plague bacilli. The culture tubes inoculated from the right inguinal glands and from the spleen developed typical plague colonies.

*Microscopic examination.*—Sections from the hemorrhagic areas of the right inguinal glands show an abundant infiltration with plague bacilli, particularly well pronounced in some peripheral areas. Bacilli, while numerous, are not present anywhere to such an extent as to form solid, clumped masses. Even where they are most abundant there are a few cells left between them. In general, the histologic elements can be much better studied in sections of this case than in those from glands which are simply choked by solid colonies of the plague organism. The general characteristics of the gland sections are a universal hemorrhagic infiltration with marked œdema, increased diastases between the original parenchyma cells, swelling of the fibrillar connective tissue reticulum, the presence of numerous leucocytic elements, and great dilatation and engorgement of the vessels. Both in transverse and in longitudinal sections of small veins, considerable damage to the vessel wall is

manifest. The cells forming these walls show coagulation necrosis, hyaline degeneration, and more or less complete loss of their nuclei. The perivascular concentric fibers are loosened and pushed apart from each other by a leucocytic infiltration. The lumina of these very much dilated vessels are crowded with apparently normal red blood corpuscles, and with a slightly increased number of leucocytes. Plague bacilli are not seen in the vessels. The original parenchyma cells, the small mononuclears, show as a rule, a normal nucleus. In some nuclei there is considerable pyknosis, while others are quite poorly stained. Mononuclears, with large hyaline protoplasmic bodies, are only rarely seen, plasma mast cells likewise are scanty. The very numerous polynuclears are generally of the ordinary type, a few are typically coarsely granular eosinophilics, while some have an angular vacuolated protoplasm which does not show any granules but stains very deeply with eosin. The infiltrating, extravasated erythrocytes are mostly, to all appearances, normal; however, in some places they have become agglutinated and confluent, almost completely forming homogeneous masses, deeply staining with eosin. No complete hyaline thrombi are found in the vessels, but a few of the latter show an open network of fibrin. Such fibrin reticula are also found here and there free between the cells. In the spleen the pulp spaces show a considerable number of large, proliferated endothelial cells. These appear to be derived from the lymphatic endothelia lining the pulp spaces. They are generally phagocytic cells, containing from two to twelve and more engulfed mononuclears, polynuclears, and erythrocytes. The picture which the pulp, with its many large endothelia, furnishes is much like that seen in typical primary splenomegaly or splenic anæmia, but the generally marked phagocytic character of the large pulp cells is analogous to the condition found in the spleen in typhoid fever. Plague bacilli are found very sparingly in the splenic sections. Kidneys: The epithelial lining of the convoluted, as well as of the straight tubules, is in an advanced state of cloudy swelling and fatty degeneration. Some of the canaliculi contain a moderate amount of granular matter. The glomeruli do not show any marked changes. All of the vessels are much engorged and small subcapsular hemorrhagic areas are encountered. Liver: The veins and capillaries are dilated and they contain much blood. The protoplasm of the parenchyma cells shows fine, dust-like vacuolation; their nuclei are generally well stained. Some of the liver

cells are swollen, hazy in outline, and without nucleus. The interlobular septa contain acute inflammatory foci mostly composed of small mononuclear cells with a few neutrophilic and a still lesser number of eosinophilic polynuclears. The pulmonary sections are characterized by enormously engorged capillaries with some blood extravasated into the alveoli. In some places an increase of the interalveolar connective tissue is noticeable. Otherwise there are no important changes. The microscopic examination of the nodule found in the bladder shows it to have the structure of a subacute inflammatory focus, composed of connective tissue fibers, small mononuclears, and some polynuclear eosinophilics. Quite a number of bacilli are seen in this area. They do not retain Gram's stain; however, they appear smaller and more delicate than plague bacillus, and they stain more uniformly than the latter.

#### CASE NO. 7. RIGHT INGUINAL BUBO.

[Necropsy Protocol No. 1000. July 5, 1904. Post-mortem examination, thirty-nine hours after death, on the body of G. A., from No. 43 Valderana Street, San Nicolas; a Filipino boy about 10 years old.]

Post-mortem rigidity has disappeared and putrefactive changes are well advanced. The skin in the region of the abdomen shows green discoloration, as does also that of the neck. The right inguinal region exhibits a swelling about the size of a walnut, and here the boundaries of enlarged glands can be made out by palpation. On section, the tissues are found to be œdematous and slightly hemorrhagic. The glands are much enlarged and hemorrhagic; but their capsules can still be distinguished and they are well differentiated from the surrounding tissue. The latter is likewise hemorrhagic, but to a less degree. On the cut surface the glands of the right inguinal region appear mottled; dark-red areas predominate and alternate with grayish-white ones. Considerable turbid and hemorrhagic juice can be scraped off. The glands from Scarpa's triangle, through the abdominal ring, up into the pelvis, are swollen, softened, and hemorrhagic. The right iliac glands as well as the right retroperitoneal ones are in the same condition. The alterations found in the internal organs, not considering putrefactive changes, are as follows: Heart: Two small subepicardial hemorrhages; myocardium, soft, flabby, and pinkish-brown. The lower lobes of the lungs are bluish-purple and quite œdematous, showing a few small subpleural hemorrhages. The spleen is enlarged to twice the size of the adult organ: it is bluish-purple externally,

dark brownish-red on the cut surface, and granular; much juice can be scraped off. The trabeculae and Malpighian corpuscles are fairly well marked. Kidneys: The right kidney is much congested and dark purplish-blue; the cut surface shows injected vessels and somewhat yellowish tubules. The mucosa of the pelvis is injected and shows several hemorrhagic spots. The left kidney is also much congested, but rather pale yellowish-gray on the cut surface. The tubules are decidedly grayish-yellow and quite dull in appearance. The pelvis is smooth and not markedly congested. The ureters and the bladder are normal. The liver is rather large with rounded margins and much yellowish mottling alternating with bluish-purple areas. The cut surface is reddish-brown and the vessels much injected. The mesenteric, retroperitoneal, bronchial, and other glands are all enlarged, congested, and rather soft and juicy. There is nothing abnormal about the intestines excepting a moderate swelling of the lymph follicles. The serosa and the mucosa of the stomach are much injected; there are no hemorrhages.

*Anatomic diagnosis.*—Hemorrhagic lymphadenitis of the right inguinal glands; multiple lymphadenitis with great congestion and softening; congestion of the kidneys and parenchymatous nephritis; fatty degeneration of the liver. Bubonic plague.

Smears from the right inguinal glands show numerous plague bacilli, those from the spleen only a moderate number. Tubes inoculated from the glands developed a typical growth.

*Microscopic examination.*—The right inguinal glands and those of the chain which leads into the right iliac fossa show changes resembling those in the other cases of hemorrhagic plague buboes. The bacilli are present in very large numbers; however, solid masses of them are found only in a limited area. In general, they densely infiltrate the hemorrhagic and oedematous tissue. The tissue elements of the infected glands in this case include a very considerable number of mononuclears with a large body of protoplasm. The latter is hyaline and stains rather well with methylene blue. A number of these large mononuclear cells contain bacilli in their protoplasm, and the cells of this type are the only ones which exhibit this phagocytic tendency. That the bacilli are really inside the protoplasm and not on top of it can be seen in very thin sections from oedematous areas where isolated cells can be studied. Some of these mononuclears have engulfed other cells.



The other cells in the gland sections are of the usual type—small mononuclears, plasma cells, mast cells, and neutrophilic and eosinophilic polynuclears. A number of vessels contain a network of fibrin. Such reticula are often seen independently of vessels in several parts of the sections. A continuation of the intravascular fibrin network to the extravascular reticula is nowhere demonstrable. The kidneys show profound parenchymatous degeneration with cloudy swelling; hyaline glomerular thrombi are not found. The post-mortem changes in the renal tissues are very advanced, so that the finer histological changes are not well preserved. The liver cells are in a condition of cloudy swelling and fatty degeneration with both fine and coarse vacuolation. The interacinous connective tissue is much increased. The septa contain numerous connective tissue fibers and infiltrating inflammatory cells. This change is so pronounced as to be due evidently not merely to plague infection but to some cause acting before the latter occurred. The interlobular inflammatory foci do not show plague bacilli. The capillaries and veins are much engorged. In the spleen the boundaries of the follicles are generally sharp and the Malpighian bodies are well differentiated from the surrounding tissue. The pulp spaces, however, are not distinct, since they are densely crowded with cellular elements. The red blood corpuscles predominate in number. The different types of leucocytes include many of the large mononuclear cells with large hyaline protoplasm, staining faintly with methylene blue. In the spleen, as in the lymph glands, some of these large hyaline mononuclears contain plague bacilli in their protoplasm. A few of the phagocytes contain other leucocytes or erythrocytes. Plague bacilli are only sparingly found in the splenic sections.

#### CASE NO. 8. INGUINAL BUBO.

[Necropsy Protocol No. 965. R. F., native, female, 45 years old, from No. 33 Calle Victoria, Intramuros. Died May 7, 1904, at 11.45 p. m., said to have been sick four days. Admitted to San Lazaro Hospital on May 7 at 11.30 p. m., and died fifteen minutes later. Post-mortem examination eleven hours after death.]

The body of a strong, stout woman, about 45 years of age. Post-mortem rigidity is well marked; post-mortem lividity is extensive. There are large livid patches on the anterior surface of the thighs and trunk. No petechiæ or ecchymoses are seen. The integument shows several old healed cicatrices, which might have been produced

by a sharp cutting instrument. There are no ulcerations, wounds, or recent cicatrices. None of the superficial glands are palpable, but on being dissected out, the inguinal glands on both sides are found to be much enlarged and congested, but relatively firm and not hemorrhagic. On section, the superficial vessels discharge a moderate amount of dark fluid blood. The serous membranes are shining, very moderately injected, and the serous sacs contain small amounts of clear fluid. The pericardium is smooth and normal. The left ventricle of the heart is well contracted and the right one moderately dilated. The valve openings, the endocardium, etc., are normal. The myocardium is moderately soft, of a reddish-brown color, and not very easily torn. The beginning of the aorta is atheromatous; the coronary vessels are moderately engorged. The lungs are slightly adherent in a few places and collapsed. Their pleural surfaces are smooth and even. The lower lobes are uniformly congested; the upper ones are very moderately so and pinkish-gray in color. The former, on section, are found to be engorged with dark fluid blood and to contain little air; the latter have a moderate amount of blood and more air. The bronchi are filled with a foamy, slightly blood tinged, viscid mucus. Their mucosa is somewhat congested, as is also the mucous membrane of the trachea and the larynx. The spleen is very much enlarged, measuring 20.5 by 12 by 7 centimeters and weighing 865 grams. It has retained the general shape of the organ and its capsule as a whole is thickened and nowhere transparent, but rather opaque. The surface is in general grayish-blue with some areas which are grayish-white. A larger area of this type is found in the center of the upper surface; it is slightly raised above the surrounding tissues and quite opaque. The vessels entering at the hilum are much enlarged in caliber, particularly the veins, which are rather thin walled. The organ is quite firm in consistency. On section, the pulp does not protrude over the cut surface, but is even, quite firm, and of reddish-brown color. The trabeculae are increased in width and stand out prominently. The Malpighian bodies are not distinct. A very moderate amount of juice can be scraped off the cut surface. The kidneys are different in size, the left one being much larger than the right. The weight of the former is 165 grams and that of the latter is 120 grams. Both have smooth capsules and their external surfaces are bluish-pink in color. On section, the vessels are found to be much engorged, the glomeruli

injected, the tubules grayish-white, the pelvis smooth and slightly injected, and the cut surface dull. The liver is very firm in consistency. Its capsule is slightly uneven and finely nodular. The external color is grayish-yellow. The organ is rather small, and the left lobe in particular is flat and atrophic. The measurements are 22 by 12 (high) by 13 (antero-posteriorly), right lobe; the left lobe is only 2–2.5 centimeters thick. The weight is 1,595 grams. There is increased resistance on cutting the organ. The color of the cut surface is ochre yellow. The acini are retracted, and the boundaries are well marked by an increase in the interlobular connective tissue. The vessels discharge a moderate amount of blood. The gall bladder is distended and contains a deep golden-yellow turbid bile. Its walls are normal and its mucosa smooth. The ducts are open. The mucosa of the stomach and duodenum are moderately injected, the injection being most marked in the gastric mucosa. There are no petechiæ or ecchymoses. The uterus is small and hard; the uterine mucosa is thin and atrophic. The ovaries are small and nodular. There is no fresh corpus luteum. Otherwise the genital organs are normal. None of the internal lymph glands show marked changes.

*Anatomical diagnosis.*—Splenomegaly (primary?); perisplenitis; cirrhosis of the liver with moderate fatty degeneration; congestion and parenchymatous degeneration of the kidneys; congestion of both lungs; Banti's disease. Bubonic plague.

After the completion of the post-mortem examination, it was thought that this was not a case of plague but one of some other infection which had taken a speedy fatal termination on account of a complication with splenomegaly and hepatic cirrhosis. However, the examination of the smears made from the inguinal glands revealed the presence of very numerous typical plague bacilli. Few such organisms were found in spreads from the spleen, the liver, and the lungs, while none were found in the heart's blood. Cultures from the spleen and the lungs developed a plague growth. No bacilli grew in the tube inoculated from the heart's blood.

Tissues were taken from both lungs, the liver, the kidneys, the spleen, and the heart, but none had been taken from the glands.

*Microscopic examination.*—Spleen: The capsule is markedly thickened, consisting of connective tissue fibers, spindle-shaped cells, and occasionally an unstriped muscle fiber. An accumulation of round mononuclear cells exists at the inner surface of the capsule.

The subcapsular lymph sinus is not very distinct, though to some extent it may be recognized. The trabeculae are thickened; their connective tissue is poor in nucleated cells and consists mostly of wavy fibers. The larger arteries show considerable hypertrophy of the adventitia. The Malpighian bodies can hardly be recognized. The accumulation of lymphoid cells around the terminal arteries forming these bodies has become much rarified, the boundaries of the cells have almost completely disappeared, and they are gradually lost in the surrounding tissue. With a low power no pulp spaces can be distinguished, but with high magnification the original ones can be recognized, at least here and there, as narrow clefts. The predominating cell element in these sections is the mononuclear type, with a vesicular nucleus, a reticular chromatin, one or more nucleoli, and a protoplasmic body, generally of medium and frequently of considerable size. These cells are clearly proliferated lymphatic endothelia derived from those which lined the original normal pulp spaces. Therefore, the great increase in volume of the spleen is to be attributed mainly to an endothelial proliferation, as several writers have previously described in certain cases of primary splenomegaly (among them the author of this report). A considerable number of polynuclear neutrophiles are also found in the pulp spaces, as well as some mononuclear plasma cells. Red blood corpuscles are present to a certain extent, though they are not so numerous as in an equal area of a normal spleen. Some of the larger mononuclear endothelia are phagocytic, containing red or white blood corpuscles, or both. (None were seen which included plague bacilli.) Here and there in the sections one sees dense and more or less irregular masses about 20 to 30  $\mu$  or more in diameter, which show a marked affinity for the eosin stain. It was first believed that these were peculiar cells, but it was finally decided that they were composed of deformed, agglutinated red blood corpuscles, sometimes including a mononuclear or polynuclear leucocyte. Plague bacilli generally arranged in small groups were found in the pulp spaces or in the outer parts of the ill-defined follicles. A search for the Donovan-Leishman bodies was negative. Liver: The interlobular hepatic tissue is increased and some of the liver lobules show marked atrophy. The septa between the acini exhibit both old connective tissue fibers without nuclei and nucleated inflammatory cells. Most of the latter are mononuclears of the small lymphoid type. Plasma cells are seen only very rarely, but ordinary poly-

nuclears are fairly numerous. The interlobular inflammatory foci also contain the same type of eosinophilic masses described above as occurring in the much enlarged spleen. The intralobular capillaries are quite distended and show an increased proportion of polynuclear leucocytes. Many of the parenchyma cells are in an advanced stage of fatty infiltration and degeneration. Few plague bacilli are seen in the liver sections. Kidneys: The capsule is somewhat thickened and a few subcapsular inflammatory foci are seen. They are composed of small mononuclear and embryonal connective tissue cells. The epithelia of the uriniferous tubules are in a condition of advanced cloudly swelling or show the vacuolation of fatty degeneration. The lumina of the tubules contain desquamated cells, mere cell shadows, detritus, and granular material. A few hyaline casts are also occasionally seen staining with eosin but not with the fibrin dye. Some of the small veins contain fibrin; none, however, is found in the glomerular capillaries. The pulmonary tissue shows engorged interalveolar capillaries and in some places a broadening of the interalveolar septa. Otherwise there are no marked changes. A very few plague bacilli are found in some of the sections.

#### CASE NO. 9. RIGHT CERVICAL BUBO.

[Necropsy Protocol No. 928. C. S., Filipina, age 5 years, from 170 Estero San Nicolas. Sick five or six days; three days in San Lazaro Hospital. Died March 18, 1904, at 11 o'clock p. m. Post-mortem examination three hours after death.]

The body of a little girl well nourished. Post-mortem rigidity and lividity marked, the latter extending well over the thorax and neck. The integument in general is quite cyanotic. The cervical glands along the right side are swollen, so that the whole mass has the size of a small apple. This region shows a very intense cyanotic condition. The tissues are very œdematous, imparting a doughy, almost fluctuating sensation to the touch. The swelling shades off gradually into the surrounding areas and in fact extends over the whole of the right side of the face. The eyelids of the right orbit are somewhat swollen and œdematous and completely closed. On incising the body, a small amount of fluid blood escapes from the veins. The stomach and the intestines are much distended with gas. The gastric veins are much congested, the injection being particularly noticeable in those along the larger curvature of the stomach. The intestinal serosa likewise shows injection of its

vessels, and there are a number of dark, hemorrhagic spots, particularly on the ilium. The mediastinal, the mesenteric, and in fact all of the glands which can now be inspected, are swollen, highly congested, and dark purplish in color. The large thymus persists; it is of a dark purple color and shows a number of very dark, almost black, hemorrhagic spots. Such hemorrhages are seen also on the visceral layer of the pericardium. The coronary veins and their branches are much injected. The myocardium is fairly firm, well contracted on the left side and dilated on the right, and of a pale pinkish color. The valves are normal. The lungs are generally pinkish-purple in color and the subpleural veins are much injected. The upper lobes contain a fair amount of air, but the lower ones very little and are much darker than the former, a good deal of dark, fluid blood escaping from them on section. The bronchial glands are in the same condition as the others, being swollen, softened, and highly congested. The spleen is much enlarged, its size being more than that of a normal adult's. Externally it is dark purplish-blue. The capsule is shining and the surface slightly wrinkled. It is soft in consistency, and on section is of a brownish-red color and has a very soft pulp. The Malpighian bodies are fairly well marked, but the trabeculae are not easy to distinguish. A good deal of dark brown juice can be scraped from the surface. The liver is swollen and of a dark purplish color with an occasional alternating grayish-white area. Its margins are rounded. On section the veins are found to be filled with dark fluid blood. The cut surface is pinkish-brown in color, with some grayish-white areas. The gall bladder is deeply injected and studded with hemorrhagic areas of a deep purple, almost black, color. Its walls are much thickened, very cedematous, and almost gelatinous in character. The mucous membrane is swollen and its small vessels are so highly injected that they can be seen with the naked eye as dark red tortuous lines. The kidneys are pinkish-purple in color, with a number of subcapsular, dark, hemorrhagic areas, which vary in size from that of a millet seed to that of a pea. The capsule peels off easily, and on its removal the glomeruli are seen as dark red points surrounded by rather grayish-white areas. The tubules are grayish-white. The mucous membrane of the pelvis is smooth, but even here the small vessels are so much injected that they can easily be distinguished with the naked eye. The suprarenals are much swollen, cedematous, and

of a dark purplish-brown color. The stomach contains a few ounces of a dark greenish fluid, in which are seen grayish-white flocculi. The mucous membrane is thrown into well-marked rugæ, and is rather pale on the whole, but contains many very small, irregular hemorrhagic spots. The mucous membrane of the duodenum likewise shows numerous small hemorrhagic spots. The pancreas is normal in color and slightly softer than usual. On cutting into the cervical glands of the right side, the tissues are found so highly œdematous that they discharge a considerable amount of clear, slightly yellowish fluid. All the glands of this region are much swollen, almost black in color, and very œdematous. The deepest ones near the angle of the inferior maxilla, the submentals, are the largest of the group, being increased to the size of walnuts. The cervical glands of the left side likewise show a good deal of congestion and œdema; however, they are small when compared with those of the right side. The inguinal glands of both sides are swollen, congested, and œdematous. In fact, all of the glands of the body which are examined during the post-mortem are in this condition. The trachea, larynx, and esophagus are highly congested. On inspection of the mouth it is found that the front teeth are small, irregularly set, and partly decayed. The right side of the soft palate is completely perforated by an ulcer which has destroyed most of the tissues forming the pillars of the fauces. The margins of the ulcer, which is about 2 centimeters in diameter, are irregular and somewhat raised. Contracted cicatricial tissue is found in the neighborhood of the ulcerations.

*Anatomic diagnosis.*—Perforating ulcer on the right side of the soft palate; general hypertrophy; congestion and hemorrhagic œdema of the general lymph glands of the body; œdema and congestion of the lungs; congestion and parenchymatous degeneration of the kidneys; œdema of the gall bladder; multiple subserous and submucous hemorrhages; syphilis hereditaria tarda. Bubonic plague.

Smears from the different organs show the following: Those from the lungs a moderate number of typical plague bacilli; from the liver a somewhat larger one; and from the spleen an enormous number, these last showing the bipolar staining in a typical manner. In the preparations the common involution forms of the bacilli are also to be observed. Smears from the cervical lymph nodes show a large number of bacilli.

Agar culture tubes inoculated during the post-mortem examination from the heart's blood, the liver, and the spleen developed typical plague cultures.

*Microscopic examination.*—Sections from the submental glands of the right side show much enlarged and congested vessels, general œdema, areas of blood extravasation, varying from the accumulation of a few red blood corpuscles to extensive and widely spread hemorrhagic areas. The finer structures of the gland are almost completely obliterated and the cortex and medulla are indistinguishable. The gland cells are mostly of the usual mononuclear type. Here and there plasma cells are found. Eosinophilic polynuclears are very scanty. The vessel walls show little or no change, appearing fairly normal even in the middle of areas of extravasated blood. Hyaline thrombi are not found in the glandular vessels. The whole of the tissue is densely infiltrated with innumerable plague bacilli, which are characteristic in shape and show polar staining. The capsule and the surrounding areolar tissue are œdematous and infiltrated with blood. The whole periglandular tissue is completely permeated by a cellular exudate. At the hilum the vessels are enormously enlarged and the perivascular tissue is increased and quite œdematous, so that the individual connective fiber tissues are separated by wide diastases. In spite of these profound changes, there is comparatively little advanced coagulation necrosis and areas where the nuclei have lost their staining properties are few and far between. In the spleen the Malpighian corpuscles are generally distinct in outline, although in some of them the boundaries have become indefinite. Here and there one of the corpuscles shows a proliferating center with large mononuclears, but without mitotic figures. The pulp spaces are not distinct because of dense crowding with erythrocytes and leucocytes. Among the latter there are seen small mononuclears, ordinary polynuclears, and a considerable number of eosinophilic polynuclears. There are also found fairly numerous large mononuclears with large, round, vesicular nuclei and a protoplasm which stains to some extent with methylene blue, though not as markedly as the plasma cells. Some of these cells show two nuclei; they are very probably proliferated endothelial cells. None of them in this case show phagocytic properties. Numerous plague bacilli are found in the pulp spaces, but very few, if any, in the corpuscles. The thymus shows the normal lymphoid tissue with included con-



centric bodies of Hassall; no atrophic changes are yet noticeable. A very prominent feature of sections of this gland is the presence of very numerous plasma mast cells with large, eccentrically situated vesicular nuclei and many coarse basophilic granules. The gland tissue proper does not contain any extensive areas of extravasated blood. However, the capsule and the periglandular loose areolar tissue show considerable blood extravasation. Only very few bacilli can be found in these sections. The renal tissue shows a moderate degree of cloudy swelling. Many of its tubules are more or less completely filled with a granular material, some of them containing hyaline casts. A moderate number of glomerular vessels show hyaline (fibrin) thrombi. Nowhere is this thrombosis very extensive or at all complete; it affects only a minor part of the vessels of one glomerulus. The renal vessels in general are very much congested, and a very few small areas of blood extravasation are found. The few bacilli which are visible are found in connective tissue—lymph clefts or in the capsular space of a glomerulus, but not inside of blood vessels. The liver shows a few small interlobular inflammatory foci and a moderate degree of fatty degeneration of the parenchyma cells. The interlobular capillaries are much distended with blood. No areas of free blood extravasation are seen. The mucosa of the gall bladder is practically normal, although the walls of the organ are intensely cedematous. The cedema and extravasated blood have infiltrated the connective tissue so extensively that the fibers form a loose open network, the meshes of which are filled with numerous pale, red blood corpuscles. From the erythrocytes the infiltrating fluid has extracted almost all of the hemoglobin, so that they do not stain well with eosin. The veins in the mucosa of the stomach are much dilated and are frequently surrounded by small periphlebitic areas of cell infiltration. The congestion of the veins of the submucosa is continued into the interglandular capillaries, from which blood extravasation has infiltrated the tissue. Some of the extravasated blood is found between the fixed cells of the mucosa, some of it being deposited free on the surface. The picture seen in these sections is very much like that found in a menstruating endometrium. Sections from the lungs, the heart, and the pancreas do not show any pronounced changes. The hemorrhagic areas in sections from the different organs were carefully examined for plague bacilli, but none were found. Hence the changes must be looked upon as due to toxic

effects and not directly to the presence of the bacilli. In fact, even in the large hemorrhagic areas of the lymph glands bacilli were practically absent, though they abounded in the neighboring ones formed by the fixed tissue elements. Stress is also to be laid upon the fact that these organisms, as a rule, were not found in the blood vessels of the sections examined. The perforating ulcer of the soft palate, surrounded by cicatricial tissue, in connection with the defective incisors, suggested the diagnosis of syphilis hereditaria tarda. It appears that the chronic syphilitic perforating ulcer became the portal of entrance for the plague virus.

### INSECTS AS PLAGUE CARRIERS.

Among the plague cases investigated there is one in which it appears probable that the infecting bacilli were carried into the body of the patient—a child—by *Pediculi capitis*. It is advisedly stated that this mode of infection appears very probable, because it is naturally impossible beyond doubt to be certain as to such an occurrence. Only experimental trials on human beings could firmly establish the possibility of this mode of transmission; but such tests with plague bacilli are of course inadmissible.

The question whether insects, and particularly parasitic ones, play a more or less important role in the spread of plague is still far from being definitely settled, as the views of investigators and writers upon this subject are diverse.

Among the modern workers on plague who first gave their attention to insects as plague carriers is Hankin, who reports on a long series of researches on the relation of ants having fed upon rats dead of plague to the possible spread of the disease. He found that ants neither die from plague nor retain the infection for any length of time. By preparing extracts of ants shortly after they had fed upon rats dead of plague, Hankin obtained a fluid which, when injected into rats and mice, would kill and produce typical plague lesions in these animals.

Ogata, in studying a plague epidemic in Formosa, took seven fleas from a rat dead of plague, crushed them between sterile slides, and injected the material so obtained into two mice, one of which died, while the other remained well.

La Bonadiere and Xanthopulides, as they maintain, by cultural methods demonstrated the presence of plague bacilli in a mosquito (?) (moustique) which had bitten a patient sick with plague.

Simond is inclined to attribute much importance to rat fleas as plague carriers. In fleas taken from rats infected with the disease he found bacilli similar morphologically to those of plague. He inoculated three

mice with material obtained from such fleas, but only one of them died, the other two survived.

Loir goes so far as to see the principal intermediary carrier of plague between rat and man in the flea. But, as Galli-Valerio has pointed out, Loir has really no valid experiments to support his claim, which he sees fit to bring forward as a demonstrated fact.

Kolle has systematically attempted to infect healthy rats from those sick with or dead of plague through the agency of fleas. However, he has never succeeded in transmitting plague in this manner, though he was able to demonstrate that fleas had really traveled from the sick rats to the healthy ones. From his observations on rats he thinks that the disease spreads among these animals because the living eat the cadavers of the dead of their own kind and not because of fleas which pass from the plague-sick to the healthy individuals. The primary bubo in rats dead of plague is generally found in the submaxillary region, which points to an infection through a slight lesion of the buccal mucosa. Kolle, in speaking on this subject, very properly remarks: "It is clear that plague bacilli will enter the body of parasitic insects which suck the blood of animals sick with the plague. It has, however, not yet been shown beyond doubt that the bite of such parasites will infect other healthy animals."

Nuttall made experiments to clear up the question as to what part insects play in the spread of plague. He demonstrated that when flies had been fed on material containing plague bacilli they still harbored the virulent organisms twenty-four and even forty-eight hours after the last feeding. According to this author, the danger of a spread of the disease through bedbugs is negligible. The evidence in favor of the "flea hypothesis" as far as the spread of plague is concerned, Nuttall considers worthless and unable to withstand scientific criticism. He states that all of his attempts to infect rats or mice through the bite of freshly infected fleas have proved futile.

Galli-Valerio severely and justly criticises the evidence so far brought forward to show that rat fleas play the most important part in the dissemination of plague among the human inhabitants of a district infected with this disease. He particularly shows that most of those who, on very insufficient evidence, assumed that fleas from rats spread the plague among human beings, have not even ascertained whether the species of fleas infesting the rats will bite man. Galli-Valerio found *Typhlopsylla musculi* and *Pulex fasciatus* on European rats and mice under normal conditions. He allowed himself to be invaded by fasting individuals of these two flea species, but neither of them bit him. By this investigator *Pulex serraticeps*, the flea infesting dogs and cats and which occasionally bites man, was not found on rats.

Tidswell, who made his observations during the latest plague epidemic at Sydney, reports that he collected one hundred fleas from rats, of which ten were identified as *Pulex fasciatus*, eight as *Typhlopsylla musculi*, one as *Pulex serraticeps*, and eighty-one as *Pulex pallidus*. The last one, it appears, has not previously been mentioned as occurring on ordinary

rats; its stated hosts are, according to Thompson, *Mus albipes* of Socotra and *Herpestes ichneumon* of Egypt. This species, the author states, bit human beings in laboratory trials, as did also *Pulex fasciatus* on one occasion. *Typhlopsylla musculi* did not bite.<sup>1</sup>

Thompson, who, during the Sydney epidemic, observed blebs which he considered to be produced by fleas and to be the place of entrance of the plague virus, concludes that the transmission of plague from rats and mice through the intermediation of fleas must be frequent.

Zirolia believes that plague can easily be spread by fleas. He observed *Pulex irritans* and *P. serraticeps*, after they had been fasting for some time, to suck blood from a plague-infected mouse, and he found living, virulent plague bacilli in the bodies of these fleas seven to eight days thereafter. Zirolia also says that the feces of fleas from plague-infected animals contain virulent bacilli, and that in the bodies of the dead fleas these parasites survive for a long time.

Maxwell, from his observations made at Changpoo, China, states that he is coming more and more to doubt the rat-flea theory. "I can not see," he says, "how we can escape plague. I must have been bitten, in spite of flea powder, many times off plague patients and so must my students. The Chinese, especially the women, catch the fleas and kill them with their teeth. If they catch fleas with plague bacilli in them, how do they escape?"

The Indian Plague Commission, which studied plague in all of its phases in India, has also looked into the question of insects as carriers of the disease, and in its report states that Simond's endeavors to establish the proposition that suctorial insects play an important part in the transfer of plague from sick to healthy animals is so weak as hardly to deserve consideration. The experience of plague hospitals in India, and especially that of the Arthur Road Hospital at Bombay, seems to indicate very clearly that suctorial insects do not come into consideration in connection with the spread of plague. The staff and attendants in the Arthur Road Hospital (where thousands of plague cases are treated) were continually bitten by insects, especially mosquitoes, and yet no cases of transfer of the infection from the sick to the healthy came under observation.

The commission also states on reviewing all the facts which have come to its knowledge, that it has little reason to suppose that ordinary, casual contact with plague-infected rats, dead or alive, is especially liable to convey the disease. On the other hand, examples are known of cases where the bite of plague-infected rats and other animals has conveyed the disease.

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<sup>1</sup> Galli-Valerio, trying to invalidate Tidswell's observations, says that this author, like others, failed to transmit plague from rat to rat through the agency of fleas and proposes the question: "If the transmission is so difficult from rat to rat, why, on the other hand, should it be so frequent from rats and mice to man, who is not as a general rule attacked by mouse and rat fleas?"

However, the report of the commission does contain some information which suggests that pediculi may be factors in the spread of plague. According to the Bombay statistics of the plague epidemic of 1896, the rate of mortality per 1,000 individuals among the Jains<sup>1</sup> of that city as compared with that among other castes is surprisingly large, and it is believed to be due to the fact that animal life is sacred among the Jains. "They will not," the report states, "sweep their staircases, or sweep their sleeping rooms, or their cooking rooms very often, lest they should destroy some animal life, so scrupulous are they. \* \* \* Not that their places are very dirty. They are a wealthy people, and their places look comparatively clean. \* \* \* The Jains, owing to their aversion to taking life, are said to be infected with parasites."

### A NEW SPECIES OF RAT FLEA.

As yet much evidence certainly has not been presented in favor of the theory that the most important intermediaries in the spreading of plague from rats to man are fleas from plague-infected rats. Even if rat fleas should have played an important rôle in the spread of plague in Sydney, as maintained by Tidswell and Thompson, their conclusions can not be generalized. How necessary it is to study this question in every place where plague occurs endemically or epidemically is shown by our observations of the rat fleas in Manila. Looking into this subject, we found, somewhat to our surprise, that the fleas infesting rats are not identical with those which have been described for other countries. Indeed, the species found here on rats appears to be new. Previous to the time when the writer began to collect rat fleas, Dr. W. B. Wherry, bacteriologist of this Laboratory, had already collected eight, which he kindly placed at my disposal. Thirty-four were subsequently caught. It is not easy to procure a large number of rat fleas, because, when the rodents have been caught, by the time they are killed and examined, the fleas have left them. For this reason Dr. Wherry succeeded in obtaining only eight fleas from fifty-three rats; while the thirty-four others were subsequently obtained from about one hundred animals. A few of the parasites were procured alive, were kept in a glass vessel for some time, and were then given an opportunity to bite both Caucasians and native Filipinos. In not a single instance did any of these fleas bite human beings. We have also collected a number of fleas from

<sup>1</sup> Average mortality per 1,000 males in the plague epidemic of 1896 at Bombay, 2.63; per 1,000 females, 1.88; per 1,000 male Jains 8.69; per 1,000 female Jains, 6.77.



persons working in the old laboratory, where numerous animals were kept and where large numbers of rats were sent for examination for plague infection; these fleas proved to be *Pulex irritans* and *Pulex serraticeps*. The flea occurring on rats in Manila was never found on human beings.

I am indebted to Mr. W. Schultze, assistant entomologist of this Laboratory, for the greater part of the following description of the flea found on rats in Manila:

*Pulex philippinensis*, sp. nov., Manila, July 19, 1904.

Head, with very small bristles; front of head high and rounded. Eyes round. Above the latter and directed backward are the antennæ, which are club shaped and consist of three segments. First and third segments equal in size; the third segment cup shaped; the second segment very small. Superior maxilla elongated, triangular. Palpi maxillarum consist of four segments, of which the last is the longest. The posterior margins of the thoracic segments possess each a row of fine bristles, as do also the abdominal ones. On the latter the bristles extend from the back downward to the middle of the abdomen, and from below upward. On the back, on the posterior margin of the eighth abdominal segment are two large bristles. In the male, below the external genitals, two large bristles on each side—i. e., four in all. Abdomen of the male bent upward. In the interior of its abdomen are the spinally curved internal sexual organs, more or less distinct in different individuals. The abdomen of the female is oval and egg shaped. Bristle on the ninth segment around the external genitals. In the abdomen of the female between the seventh and the eighth segment is an intestine or sausage-like curved organ—the ovary. Behind it in one individual are several barrel-shaped ova.

The longest bristles are found at the lower ends of the femora. They measure 0.2 millimeter in the female and 0.15 millimeter in the male:

Color: Light reddish-brown.

Size of the female: Length, 1.8 to 2.67 millimeters; breadth, 0.80 to 1.25 millimeters.

Size of the male: Length, 1.16 to 1.78 millimeters; breadth, 0.70 to 0.75 millimeter.

Size of the ova: Length, 70  $\mu$ ; breadth, 55  $\mu$ .

Types in the collection of the entomological division of the

Biological Laboratory, Bureau of Government Laboratories, Manila, P. I.

*Pulex philippinensis* appears to be a stationary parasite of the rat; it is found in Manila. It is much like *P. anomalus* recently described by Baker and found by him in California. However, the head, eyes, antennæ, palpi, and bristles offer marked points of differentiation.

It is of interest to mention that Baker in his monograph on American Siphonaptera describes a new species of rat flea from Brazil, South America. It is a very large one, the male being 3.5 millimeters and the female 5.5 millimeters in length. Evidently there are several different species of rat fleas in different parts of the world.

#### EXPERIMENTS WITH FLIES.

Experiments which have been made to demonstrate that plague may be spread by flies are all inconclusive, because the arrangements were such that the transmission of the disease was inevitable. Flies were fed with bouillion containing plague bacilli and after varying intervals of time had elapsed were ground up. The emulsion so obtained was subsequently injected into guinea pigs or rats, which of course died of the disease. Such experiments can not determine with certainty whether plague can or can not be carried by flies.

Experiments were therefore conducted which were designed more closely to imitate what might take place in nature. The organs of plague cases, both from man and from guinea pigs, were kept in an anatomical jar, over which was placed a flytrap containing a number of flies. The door of the trap was then opened and the flies allowed to come in contact with the plague organs in the lower vessel. After they had remained in the lower vessel for varying periods of time (from one to several hours) they were again induced to enter the trap by surrounding the lower vessel with some dark material, which caused them to seek the upper light space. The trap was then closed and placed over an especially constructed fly-proof cage, in which were two guinea pigs. The door of the trap was opened so that the flies could enter the cage. The guinea pigs had been shaved over an extensive area of the back and some sirup had been dropped on a few spots, to attract the flies and to cause them to come in contact with the bodies of the

animals. This experiment was performed twice; but in neither case did the guinea pigs contract plague. It had been proved by preliminary trials that the flies which had been allowed to come in contact with and to eat from the organs of plague cases had bacilli either in or on their bodies. Flies which had been allowed to come in contact with plague organs were then caught in the trap, chloroformed, picked up with sterile forceps and dropped into slightly alkaline bouillon; in every case a growth of plague bacilli was observed in the media in which they were placed.

Another observation, which was not made experimentally but under perfectly natural conditions, may here be recorded. The San Lazaro morgue at Manila, a building so constructed as to be insect proof, owing to the inclemency of the weather soon became in such a condition that flies could readily go in and out in large numbers. During post-mortem examinations on plague cases flies generally passed freely from the dissected cadavers to those making the examinations as well as to others present, and undoubtedly also to the outside of the building; yet no cases of plague have occurred in the part of the city where the morgue is located. However, this part of the town is only sparingly inhabited. Hence, no case can be attributed to flies as carriers of the infection.

When one takes what has been said above into consideration, one is certainly inclined to conclude that insects, as a rule, do not probably play a very important role in the spread of plague. However, the observation that this disease is exceedingly prevalent among that caste in Bombay which is probably more infected with pediculi than any other suggests that certain parasites may be operative in its transmission. As stated in the remarks introductory to this part of the paper, one of the cases here observed strongly suggests that pediculi may be carriers of the infection.

#### **A CASE OF BUBONIC PLAGUE IN A CHILD, IN WHICH THE INFECTION WAS POSSIBLY CARRIED BY PEDICULI.**

##### **CASE No. 10. CERVICAL BUBO.**

[Necropsy Protocol No. 910. C. S., a Filipina girl, 9 years of age, from Anda Street, Intramuros, Manila. Post-mortem examination five hours after death, on Saturday, March 5, 1904, at 4 p. m.]

The body of a female child, 9 to 10 years of age, well developed. Post-mortem rigidity strong. Post-mortem lividity well marked and extending over the sides of the body, being particularly notice-



able around the neck. The cervical glands on both sides are swollen, imparting a doughy sensation to the touch. The tissues in the neighborhood of the swollen glands are quite cedematous. The integument of the body shows no lesions. There is no discharge from the ears; nor does the external meatus on either side show any ulceration. The mucous membrane of the buccal and nasal cavities is congested, but otherwise normal. The scalp is infested with numerous pediculi, which seem to be ill at ease and run about as if disturbed. On section the superficial veins of the body discharge a moderate amount of very dark, fluid blood. The heart is normal, except that the superficial, subepicardial veins are much injected. The myocardium is somewhat soft, dull, and rather pale pinkish-yellow in color. The lungs are pinkish-purple. The lower lobes on the cut surface are dark reddish-brown, containing much dark, fluid blood and little air. Some of the areas seen on section are in a condition of almost red hepatization, containing a very large amount of dark, fluid blood. The mucous membranes of the bronchi are slightly swollen, hyperemic, and moist. The tracheal mucosa is in the same condition. The larynx is much injected, particularly the epiglottis. The bronchial glands are dark purplish, slightly swollen, and somewhat softened. The spleen is of medium size. The capsule is smooth as a whole, though slightly wrinkled and grayish-blue in color. The cut surface is reddish-brown. The trabeculae are well marked; the Malpighian bodies are fairly well visible. The mesenteric glands are reddish-purple, swollen, and rather soft. Both kidneys show fairly numerous subcapsular hemorrhagic areas, varying in diameter from about one-half centimeter to a mere point. The capsules peel off easily, and after their removal the surfaces show alternating areas, either deeply injected or grayish-yellow. On section the vessels appear highly congested and the glomeruli stand out as deep reddish-yellow points. The tubules are grayish-yellow; the pyramids are deeply injected. The mucous membrane of the pelves is smooth and slightly swollen, but not hemorrhagic. The substance of the kidneys is soft and almost gelatinous. The suprarenals are large, swollen, congested, and very soft. The surface of the liver is bluish-pink, mottled with pale grayish-yellow areas. The capsule is smooth. The cut surface is grayish-yellowish-pink. The veins contain a good deal of dark, fluid blood. The gall bladder contains a turbid, yellowish

bile. The mucous membrane is smooth. The serosa of the stomach and intestines is injected. The superficial veins are marked as reddish lines. The mucosa as a whole is moderately injected, with punctiform hemorrhages in the ventricular portion. The intestinal lymph follicles are somewhat swollen. The peritoneal covering of the uterus and tubes is much injected. All of the fine superficial vessels are visible in consequence of the marked congestion. The cervical glands on both sides, including those along the sternocleido-mastoid muscles and the deeper submental ones, are enlarged, highly congested, and softened. On section a good deal of dark, bloody fluid can be scraped from the surface.

*Anatomic diagnosis.*—Hemorrhagic, acute, parenchymatous nephritis; congestion and œdema of the lungs; moderate fatty degeneration of the liver; hemorrhagic inflammation, hypertrophy, and softening of the cervical glands on both sides; more or less general hypertrophy of most of the lymph glands. Bubonic plague.

Smears from the cervical glands show numerous plague bacilli, but those from the spleen only a moderate number.

Before the body had been opened, three pediculi were picked up from the scalp with sterile forceps and dropped first into an empty sterile test tube and later into three flasks containing 50 cubic centimeters of sterile, slightly alkaline bouillon. All of the three flasks developed cultures of plague bacilli. The cultures were then transferred to various media and the bacteria were fully identified as typical plague organisms. One culture from the spleen and two from the cervical glands likewise developed plague bacilli.

Since this child, dead of bubonic plague, had come from a district which had been considered plague free for some time, inquiries were made as to the possibility of the girl's having been infested with pediculi from some one living in an infected district. Dr. R. E. S. Newberne, district medical inspector, reported on the matter as follows:

So far as the records show, only two cases of bubonic plague, prior to the one under discussion, have occurred on Calle Anda, the first in 1900 at No. 11, and the second in 1901 at No. 137. These numbers being at a considerable distance from No 89, and in opposite directions, it may be assumed that the district is not infected. The orphan, C. S., was taken to 89 Anda from the Hospicio de San Juan December 24, 1903, and remained in good health until the last days of February, when she became ill,

complaining of carache and fever, which did not yield to local treatment. The patient was sent to San Juan de Dios Hospital about March 4, where she died twenty-four hours later, after an illness of nine days. So far as can be ascertained, this child did not handle rats or do anything else to which infection could be ascribed. She slept on a petate on the floor of one of the upstairs rooms, as is the native custom. With the exception of the time from the 7th to the 16th of February, when she attended the public school on the corner of Victoria and Magallanes, she did not associate with children outside her home. The family assert that she was free from vermin when she was sent to the hospital, though it was admitted that Filipino children are generally infected with *Pediculi capitis*. Five bedbugs found in a crack of the floor upon which she slept and thirteen rats, only one of which was found alive, were sent to the Laboratory on March 11 for examination.

Mr. Chas. B. Hare, assistant bacteriologist in this Laboratory, who examined the rats, did not find any evidence of plague in them. Smears were made from the five crushed bedbugs, which likewise did not show any plague bacilli. It was intended to test the bedbugs by cultural methods, but this was overlooked by mistake.

*Microscopic examination.*—Sections from the cervical glands show, even on a superficial examination, a number of most profound changes, namely: (1) Almost complete loss of the normal structure and differentiation of the gland into cortical follicles and medullary cords; (2) advanced coagulation necrosis; (3) extensive extravasation of blood; (4) deposit of granular and fibrillar fibrin; (5) the presence of enormous solid, irregularly distributed masses of bacteria. The deeper portions of the cortex still present some oval compartments outlined by fibrous connective tissue, evidently once the trabeculae; however, the latter do not contain normal lymph follicles, but masses of necrotic tissue and free extravasated blood. Where the dense masses of bacilli are located, there are few tissue elements left. The cells which are still recognizable as such are the mononuclears; their nuclei generally show a marked pyknotic condition. At the margins of the bacillar masses and clumps are mononuclear cells more normal in character, among which are found quite a few polynuclear eosinophiles. Almost as numerous as the latter are the plasma mast cells. The bacilli are found also in the tissues, next to the large colonies; here the micro-organisms do not form solid, dense masses, but are freely distributed among the cells. Intimately mixed with the leucocytic cells and the bacilli are numerous red blood corpuscles. The peripheral tissue,

next to the capsule, shows a dense infiltration with completely degenerated erythrocytes and contains hematoidin and hemosiderin. This zone appears as a part of the former lymph sinus; however, this can no longer be distinctly recognized as such. Here, likewise, numerous bacilli are found. Fibrin is quite irregularly and extensively distributed throughout the gland. In its interior it is observed to be in the form of a granular deposit and also in the shape of finer or coarser threads. Around the dense masses of bacilli it occurs in the form of fibrillar network, sending fine threads into the masses of micro-organisms. The tissue next to the capsule—i. e., the former lymph sinus—likewise contains a network of fibrin. The small vessels are more or less completely occluded by hyaline (fibrin) thrombi, which are seen both in the interior of the gland and in the capsule. Here and there the fibrin extends from the interior of the vessel, through its wall, into the perivascular tissue. In the blood vessels bacilli, if found, are present in scanty numbers.

**Kidneys:** The renal tissue presents a most striking picture. Sections from both kidneys, treated by Weigert's fibrin method, appear as if the vessels had been injected with a violet-stained gelatin. There is not a normal glomerulus to be seen. All the sections show a more or less complete obliteration by hyaline thrombi. In most of the Malpighian bodies the hyaline thrombosis of the capillaries is so perfect that both the main branches of the afferent vessel and the smaller capillaries given off from the larger loops are sharply outlined. Most of the thrombi appear perfectly solid; however, some are hollow in the center, as can be seen both in transverse and in longitudinal sections. The endothelial lining of the thrombosed vessels is well preserved. Where the thrombi are comparatively thin, one can see, both in the transverse and in the longitudinal sections, endothelia which are perfectly normal to all intents and purposes. Nowhere do the thrombosed vessels to any extent show a loss of endothelia. Therefore, the thrombosis can not be attributed to a denudation of the vessels of their endothelial lining. The capsules of Bowman are likewise normal, though a few of them show a very moderate amount of thickening; their lining epithelium exhibits no marked changes. In some places the hyaline thrombi are continued into the vasa afferentia, and even into the vessels of which these are branches. Quite commonly there are seen between the uriniferous tubules parts of such small vessels filled with hyaline thrombi. However, none are found

in the larger arteries or veins, in some of which finely granular fibrin and desquamated endothelial cells are present. The vessel walls themselves show no damage aside from a minor degree of denudation of the intima. There is in particular no extension of the fibrin through the vessel walls, nor is there any evidence of mesophlebitic or periphlebitic—or arteritic processes. The epithelia lining the convoluted uriniferous tubules are somewhat swollen, with indistinct outlines and a vacuolated protoplasm; but their nuclei are yet quite normal. A granular material partly fills some of the convoluted tubules. The epithelial lining of the straight tubules does not show any marked changes. The capsule of the kidney is normal. Nowhere do any of the renal blood vessels show a large number of plague bacilli; a few are possibly seen inside some vascular lumina; but even this is not certain. A moderate number of bacilli are seen in the lymph clefts between the tubules and around the Malpighian bodies. A few slender, long bacilli, which retain Gram's stain, are occasionally found in the tubules; but they are probably of no significance and represent an agonal or post-mortem invasion. Sections of the liver show a very few small periphlebitic inflammatory foci composed of small, round mononuclears. The liver cells all show a coarse vacuolation, some of the vacuoles being larger than the nuclei. The capillaries are moderately filled. There is no free extravasated blood. A very few plague bacilli are found between the liver cells.

#### CASE NO. 11. RIGHT INGUINAL BUBO.

No complete necropsy protocol was kept. Body of a male Chinese, 26 years old, who died after an illness of seven days. Sections of the kidneys show hyaline fibrin thrombosis of the glomerular capillaries, with an extension into the afferent and efferent vessels as well as into the intertubular capillaries and small veins. There is general vascular dilatation and engorgement and cloudy swelling of the epithelia of the uriniferous tubules. In the spleen, which contains numerous plague bacilli, there is found a homogeneous, eosin-staining material, which is apparently derived from red blood corpuscles which have become confluent. At the margins of the homogeneous material erythrocytes singly and in groups may be distinguished. Coarse fibrin threads, forming a network, are here and there seen in the homogeneous material. Hyaline fibrin thrombi are likewise encountered in the small splenic vessels.

## GROUP II. PRIMARY BUBONIC PLAGUE WITH SECONDARY PLAGUE SEPTICO-PYEMIA.

### CASE No. 12. RIGHT INGUINAL BUBO WITH SECONDARY PLAGUE SEPTICO-PYEMIA.

[Necropsy Protocol No. 1011. M. N., Filipino male, 40 years old, from 77 Sacristia Street, San Nicolas. Ill six days; died early July 29, 1904. Post-mortem examination about six hours after death.]

The body of a middle-aged man, about 40 to 45 years old, in a fair state of nutrition, and strongly built. Post-mortem rigidity strongly marked, as is also post-mortem lividity on dependent parts. There are no wounds or abrasions. The right inguinal glands are swollen. Here the tissues are hard, infiltrated, and œdematous. Individual glands are not distinguishable. None of the other lymph glands, with the exception of the left inguinal ones, are palpable. Much dark, fluid blood escapes from the vessels when the body is opened. All the serous membranes are highly injected and reddened and numerous hemorrhages, to be more fully described, are seen. The pericardium, aside from congestion, is normal. The heart shows a number of subepicardial hemorrhages, varying from one to several millimeters in diameter. The left ventricle is well contracted and the right one dilated. The myocardium is rather soft, pinkish-yellow, and dull in appearance. Otherwise the heart is normal. The beginning of the aorta presents several raised, hard, atheromatous patches. The lungs are heavy and externally are bluish-purple, with black patches and subpleural hemorrhages. The right apex is adherent and consolidated, and at its very point there is an emphysematous cystic bladder of the size of a hazelnut with a smaller one of the size of a pea. These vesicles contain air and collapse on being cut in to. The apex as a whole is consolidated, and this area contains fibrous and calcareous nodules. The lungs, on section, are generally dark brown and contain much blood and œdematous fluid. The bronchial, tracheal, and laryngeal mucosa is moist, swollen, and deeply injected. The epiglottis is uneven and dark red in color. The papilla circumvallata of the tongue are much swollen. The spleen is enlarged to from two to three times its normal size and is firm in consistency. The capsule is smooth and steel-grayish-blue. The cut surface is smooth and rather light brownish-red. The pulp is not softened and does not protrude. The trabeculæ are easily visible; the Malpighian bodies are less so. The kidneys are normal

in size. The capsule is smooth and in general grayish-blue in color, with numerous and large subcapsular hemorrhagic areas. On section the vessels are engorged, the tubules grayish-yellow, and the surface dull in appearance. The pelves are smooth but highly injected, with several hemorrhagic spots. The ureters likewise show hemorrhages. The bladder is contracted and its wall firm; its serosa is highly injected. The mucosa is swollen, congested, and studded with small hemorrhagic spots. This organ contains 25 to 35 cubic centimeters of a coagulated, gelatinous, bloody material.

**Liver:** The capsule is smooth and pinkish-purple, with a good deal of yellow mottling. There are confluent, subcapsular hemorrhagic spots on both sides of the insertion of the suspensory ligament. The consistency is increased, the elasticity decreased. The cut surface is ocher-yellowish-brown in color and very dull, as well as slightly uneven. The vessels contain much dark blood. The wall of the gall bladder is deep green with black hemorrhagic spots. It is thickened, oedematous, and almost gelatinous. The viscus contains a moderate amount of thickened, almost black, pitchy bile.

**Stomach:** The serosa is injected and shows a number of hemorrhagic spots. The walls as a whole are thickened. The contents of this organ consist of a dark coffee-brown, grumous mash. The mucosa is swollen and all the vessels are injected. The whole surface is studded with small hemorrhagic dots. On the posterior wall, not far from the pylorus, there is a perfectly smooth cicatrix with radiating lines; however, this is not at all well marked and can be seen only on close and careful inspection. There is a fairly hard nodule, not larger than a pea, in the circumference of the pylorus; it is not well differentiated from the neighboring tissue, and shades off gradually. There is no ulceration in the region of the pylorus and the mucosa above the described nodule shows no changes beyond congestion, etc. The esophageal and duodenal mucosa likewise shows great congestion and hemorrhagic spots. In the large intestine there are found a number of dark, submucous nodules of the size of a pea; they contain dark, partly coagulated blood. The intestinal follicles are swollen. The tissues in the right inguinal region on being cut discharge a considerable amount of blood-tinged serous fluid. The glands are swollen, completely hemorrhagic, and generally indistinguishable as to outline. The capsules are only exceptionally recognizable, and as a rule the whole tissue forms one undifferentiated, bloody mass. The

bloody infiltration is extensively continued into the surrounding tissue. The whole inguinal region is adherent to the overlying skin. The hemorrhagic condition is continued into the inguinal canal. The whole chain of glands, the right iliac, the retroperitoneal, the abdominal, the aortic, etc., is in a state of hemorrhagic inflammation. The areolar tissue of the left side of the pelvis and the abdominal cavity is œdematous, gelatinous, and extensively infiltrated with blood. The sheaths of some of the pelvic and abdominal vessels show hemorrhagic infiltration, as does also the loose tissue around the right kidney and the gall bladder. Except where specifically mentioned, the glands are all swollen, softened, and at least highly congested, if not hemorrhagic. Smears from the right inguinal glands show numerous plague bacilli. The organisms are also present in moderate numbers in those from the spleen.

*Anatomic diagnosis.*—Congestion and œdema of the lungs; hemorrhagic, acute, parenchymatous nephritis; parenchymatous and fatty degeneration of the liver; hemorrhagic inflammation of the right inguinal and many other lymph glands; extensive subserous, submucous, and interstitial hemorrhages. Bubonic plague.

The cultures inoculated at the post-mortem examination developed a typical growth.

*Microscopic examination.*—Upon a general survey, the glands of the right inguinal region show an extensive hemorrhagic infiltration with much necrosis, particularly in those places where the extravasation is the greatest. The normal gland structure in general has disappeared, but here and there follicles may still be recognized where the blood extravasation is not so extensive. All vessels are much dilated and engorged. The connective tissue at the hilus is greatly increased. The capsules of the glands are loosened by a hemorrhagic œdema: and their cells as well as those of the connective tissue reticulum of the glands themselves are swollen and even completely necrotic. The periglandular, loose, areolar tissue is likewise hemorrhagic and in part distinctly necrotic. If the vessel walls are examined with a high power, it is seen that they are rarified by an œdematous infiltration. The cells forming them either show no nucleus at all or a poorly stained or a pyknotic one. The same changes are noticeable in the capsular and periglandular vessels. A number of the parenchyma cells, outside the zone of the dense bacillar zooglea masses, consist of fairly normal, small



mononuclears. Others of this type show a swollen protoplasm with either a poorly stained nucleus or one not stained at all. Bodies are also present which may best be described as cell shadows, which contain a rather fine, dark brown, granular pigment, probably a hemoglobin derivative. Coarse and fine granular, yellowish-brown pigment is also seen between the cells. Typical plasma cells, mononuclears with a large hyaline protoplasm, and polynuclears are not numerous. Eosinophiles are not seen. A few small vessels contain hyaline fibrin thrombi; but there is no extravascular fibrin reticulum present. Plague bacilli are found in dense masses, in which only a few autochthonous tissue cells are left and those greatly changed. From the dense clumps the bacilli infiltrate the spaces between the cells in those parts of the sections where more cells are still present. Spleen: The capsule shows no marked changes; the trabeculae, on the other hand, generally show hyaline swelling and loss of nuclei. A small trace of an original Malpighian body is seen here and there. Most of the corpuscles have disappeared in consequence of necrotic processes, or at least their boundaries have become quite indistinct, the follicle losing itself in a dense mass of changed nucleated cells and degenerating erythrocytes. The pulp spaces are indistinguishable on account of their great engorgement with blood. Everywhere there is present a homogeneous mass with vacuoles, which are more or less occupied with nucleated cells. The homogeneous matrix, which stains well with eosin (in some places it takes the stain particularly well), is very probably a product of degenerated, agglutinated, confluent red blood corpuscles. In fact, in some places the more or less homogeneous, eosin-staining material is undoubtedly composed of red blood cells. The cells found in the vacuoles of the homogeneous matrix are mostly polynuclears. Next in order of frequency come small mononuclear cells. These show more marked changes than the former, namely, poorly stained or very pyknotic or fragmented nuclei. Eosinophiles are also found. Plasma cells and large hyaline mononuclears are not seen in the spleen. Bacilli in small numbers are scattered all over the sections, and in places are found in more numerous groups. A few small vessels contain hyaline thrombi. Kidneys: All vessels are much dilated and engorged. The interstitial connective tissue is oedematous and shows a decided increase in some places, although not so great as that seen around the capsules of Bowman. In general the glomerular capillaries are like the

renal vessels, much dilated and engorged. Hyaline fibrin thrombi are found in few of the glomeruli. The thrombosis of the glomerulus is as a rule not complete and only a part of the tuft is closed by fibrin. The thrombi are sometimes continued into the vasa afferentia and efferentia and beyond them. The capsular epithelium shows a minor degree of degenerative, but no proliferative, change. The tubular epithelium is in a state of cloudy swelling and fatty degeneration. These degenerative processes are more marked in the convoluted than in the straight tubules. Most of the uriniferous canaliculi contain an abundance of granular material, while others have casts. Sections from the kidneys show an extensive infection with plague bacilli, which is mostly localized in the glomerular capillaries. Both in the open and in the thrombosed capillaries numerous bacilli may be seen in loose groups or sometimes even in dense masses. In the thrombosed vessels the bacilli are sometimes between the thrombus and the vessel wall. The organisms occasionally extend beyond the glomerulus into the vasa recta. Here and there bacilli are found at quite a distance from a glomerulus and occasionally in the capsular space and in the uriniferous tubules. Liver: The interacinous tissue shows small, round-cell, inflammatory foci and increase of the fibrous connective tissue. The portal and hepatic veins and the interlobular capillaries are dilated and engorged, showing a somewhat increased number of leucocytes. The parenchyma cells are very coarsely vacuolated and contain much bile pigment. Here and there plague bacilli are found in the capillaries; they appear in larger, denser groups near the central vein of the lobule and near the interlobular inflammatory foci. Where the bacilli are present extensively, there are seen cells with one, two, or three nuclei with many bacilli included in their protoplasm. These phagocytic cells appear to be vascular or lymphatic endothelial cells. Lungs: All vessels, including the interalveolar capillaries, are much dilated and engorged. The alveoli are partly or completely filled with a granular, or almost homogeneous, eosin-staining material; they also contain quite a few desquamated, pigment-filled epithelial cells. Here and there extravasated blood is found in the air spaces. Fibrin is not visible in the pulmonary sections, nor are plague bacilli found. Stomach: The interglandular capillaries of the mucosa are greatly dilated, and free blood is observed between the glands. Towards the surface of the mucosa the hemorrhagic areas become larger. The most

superficial parts of the mucosa, which are strongly infiltrated with blood, are necrotic. Here we find places where the surface epithelium is missing, so that the blood is free on the surface of the mucosa. The large parietal cells are very coarsely granular and stain deeply with eosin. Some of them have two or three nuclei, while others are much swollen and have lost their nuclei. Fairly dense masses of plague bacilli are found in some of the superficial hemorrhagic areas. The nodule in the region of the pylorus of the stomach shows a mucosa in an extensive state of glandular hypertrophy. The gland formation, however, is so typical that the process cannot be looked upon as an early stage of carcinoma. It is simply a glandular hypertrophy. In the duodenum the same vascular changes are seen as in the gastric mucosa. However, the blood extravasation is very insignificant and the vascular dilatation more moderate. In spite of this, the more superficial parts of the duodenal mucosa is necrotic, not uniformly so but in small patches. Eosinophilic polynuclear are numerous in the duodenal mucosa and submucosa. Plague bacilli are not found. The dark cysts encountered in the interior of the large intestine are blood cysts formed between the muscularis and the submucosa of the bowel. The hemorrhage has completely dissected apart the muscularis and the submucosa. The contents of the cysts are pale, changed, or fairly normal erythrocytes, between which are found hyaline degenerated vessel walls and some irregularly distributed elastic fibers. The mucosa overlying the cysts is in a condition of coagulation necrosis. Plague bacilli are not found in or near these blood cysts; neither are any animal parasites encountered.

#### CASE NO. 13. LEFT SUBMENTAL BUBO.

[Necropsy Protocol No. 1027. F. C., a Filipina, 14 years old, from No. 195 Plaza Leon XIII, Tondo. Died after a short illness of unknown duration, on September 7, 1904, at 7.10 o'clock p. m. Post-mortem examination made on September 8, at 3 o'clock p. m.]

The body of a slender young girl about 15 years of age. Mammary glands fairly well developed and the pubes scantily covered with hair. The nutrition is good. There are no deformities, external wounds, sores, pustules, etc. The post-mortem rigidity is fairly strong; the post-mortem lividity is well marked on dependent parts and spreads toward the sides of the trunk. The left side of the face is quite cyanotic and swollen. The swelling is most marked underneath the parotid region; it is not sharply

defined but shades off gradually into the surrounding tissues. The swollen area is œdematous and doughy to the touch. The enlarged glands can not be distinguished well by palpation. The abdominal cavity contains a small amount of fluid. The lungs are nowhere adherent. The pericardium is normal, as is also the pericardial fluid. The right ventricle of the heart is well contracted, the left one dilated. A few small subepicardial hemorrhages are found on the surface. The myocardium is fairly firm, pink with a very faint tinge of yellow and somewhat dull in appearance. Otherwise the heart and the large vessels are normal. The coronary vessels are much congested, the two sides containing chicken-fat clots and some dark, fluid blood. The lungs are inflated, heavy, and bluish-purple on the outer surfaces. The right lung shows a number of small subpleuritic hemorrhagic spots, most of which are found at the two adjoining surfaces of the middle and the lower lobes. On section the pulmonary tissue is found to be much congested and œdematous and dark brownish-red. The bronchi contain some foamy, viscid mucus and their mucosa is slightly swollen and injected. The injection of the bronchial mucosa is very marked and the small arteries and veins are quite visible. The mucosa of the larynx is in a similar condition. The internal surface of the epiglottis exhibits about half a dozen pin-head-sized submucous hemorrhages. The bronchial glands are quite markedly enlarged, softened, and congested, those on the right side being more so than the ones on the left. Posteriorly at about the middle of the trachæ there are found two lymph glands each of the size of a bean, which are swollen, soft, and much congested. The left tonsil is swollen, hyperemic, and slightly ulcerated. The spleen is about one and one-half to two times the size of the normal adult spleen. Externally it is bluish-gray and has a smooth capsule. In consistency it is quite soft and flabby. On section the surface is granular and the pulp is found to be very soft. The trabeculæ are distinct; the follicles are very indistinct. Much brown juice can be scraped from the surface. The kidneys are quite large and fairly firm. The capsules are smooth, and the external color is pinkish-gray. Both kidneys show a few subcapsular hemorrhagic spots, the largest one being of the size of a split pea. The capsules peel off easily. On section the surface is quite dull and grayish-yellow, with injected blood vessels, which have a prominent yellowish-gray background. The glomeruli are visible as red

points. The pyramids are rather pale. The relation of the cortex to the medulla is normal. The pelves are injected but without hemorrhagic spots. The right ureter is somewhat dilated and about one and one-half times the diameter of the left one, which is normal in size. The bladder contains about two ounces of turbid, yellow urine. The mucosa of the bladder and the ureters is hyperemic but not hemorrhagic. The ovaries, the tubes, and the uterus are normal. There are no fresh corpora lutea, but the uterine mucosa is diffusely hemorrhagic. The serosa of the corpus and the tubes shows dilated and congested vessels. The suprarenals are dark brownish-yellow, fairly soft, somewhat swollen, congested, and œdematous. The gastric and duodenal mucosa is enormously congested, the former showing extensive hemorrhages in the form of densely crowded dots and irregular areas which have evidently been formed by petechiæ and ecchymoses which have become confluent. The submucous hemorrhages in the duodenum are moderate in extent. The mucosa of the small as well as of the large intestine shows a marked hyperemia, but the lymph follicles are not swollen or at most very moderately. The mesenteric and retroperitoneal glands show only very moderate swelling and congestion. The liver is of normal size. The capsule is smooth and purplish-blue with grayish-yellow mottling. The consistency is perhaps somewhat increased. On section the surface is even and yellowish-pinkish-brown. The distended veins of the liver contain much blood. In the center of the right lobe there was found a focus the size of a pea, composed of a somewhat loose, soft, grayish-white mass. The gall bladder is normal and contains some dark greenish-yellow bile. The ducts are normal. The pancreas is slightly swollen but otherwise normal. When the swollen region of the left side of the face is incised, a yellowish serous fluid escapes from the areolar subcutaneous connective tissue. The skin is firmly adherent to this tissue and can be dissected only with some difficulty. The color of the serous fluid is yellowish with a faint tinge of red. On dissecting deeper into the tissue, enlarged lymph glands are encountered, which are swollen, soft, and much congested. Glands are met with deeper down which are intensely so. The hemorrhages, however, do not extend into the œdematous periglandular tissue. The parotid gland is swollen and much congested, but not hemorrhagic. Brain: The longitudinal sinus contains a large chicken-fat clot. The pial vessels both on the convexity and at the base

are enormously congested. The brain substance shows many hemorrhagic points (small hyperemic vessels); otherwise no noteworthy changes are seen.

*Anatomic diagnosis.*—Congestion and parenchymatous degeneration of the kidneys; congestion and œdema of the lungs; one necrotic focus of the liver with congestion and fatty degeneration; multiple subserous and submucous hemorrhages; left submental hemorrhagic bubo. Bubonic plague.

Smears from the deep hemorrhagic submental glands show many typical plague bacilli; while those from the superficial, softened, and congested glands reveal only a very moderate number. In the juice of the spleen there are very few, and in that of the lungs they are exceedingly scanty. Culture tubes inoculated from the hemorrhagic glands and from the spleen developed a typical growth.

*Microscopic examination.*—Sections from the deep submental glands show a complete loss of the finer structure, extensive free hemorrhages, and the formation of a homogeneous eosin-staining material (evidently derived from degenerated blood corpuscles which have become confluent, and extensive areas of necrotic material. In the latter there are a few cells with pyknotic nuclei. Vessels are still recognizable in this necrotic mass, but merely by faint outlines, the greatly dilated walls having become much thinned and loosened. The capsule has been loosened by a cellular infiltration composed of mononuclear and polynuclear leucocytes. The infiltration extends beyond the capsule into the loose, periglandular, areolar tissue. In the outer part of the gland, the cells are better preserved and the hemorrhagic extravasation is moderate. The cells found here, aside from erythrocytes, are mononuclears and a few polynuclears. The former are mostly of the small type, although there are some large ones, with a vesicular nucleus containing a reticular chromatin and a large body which has a marked affinity for methylene blue. Bacilli are found irregularly diffused throughout the gland; they are very poorly stained, shell-like, and oval. The more superficial cervical glands are fairly well preserved in structure, showing an increase of the hilum connective tissue, great dilatation of the otherwise intact vessels, very small, scanty areas of blood extravasation, and large mononuclears with a somewhat basophilic protoplasm. Bacilli are present in very scanty numbers. No fibrin thrombi or fibrin networks are found in any of the glands. The spleen shows small, not well defined

corpuscles and indistinct pulp spaces crowded with red blood corpuscles and nucleated cells. Most of the latter are small mononuclears. Large mononuclear, lymphatic endothelia are not very numerous, a few of them containing the remnants of red blood corpuscles. A moderate number of plague bacilli are present in the sections. The vessels of the kidneys, including the glomerular capillaries, are greatly engorged and small areas of blood extravasation, both subcapsular and interstitial, are seen here and there. The uriniferous tubules show a loss of epithelium and advanced cloudy swelling with granular material in the tubular lumina. The capsules of Bowman are not thickened. There is no proliferation of the glomerular epithelium. The interstitial connective tissue is œdematous and here and there shows some finely granular material deposited between the tubules. Plague bacilli are not seen in the renal sections. The suprarenals show an enormous engorgement of the interfascicular capillaries. In the liver one sees great dilatation of the capillaries, and veins with an increased number of leucocytes in the former. The parenchyma cells are both finely and coarsely vacuolated. One of the three pieces of liver which was taken for microscopic examination shows a very small focus of coagulation necrosis. Here the parenchyma cells are completely necrotic and in fact indistinguishable. A few small mononuclears are found scattered over the necrotic focus, which also shows a reticular, finely fibrillar matrix. At the very margin of the focus is seen a multinuclear giant cell, with a crescentic arrangement of its nuclei. The large cell has the typical appearance of a giant cell in tuberculosis. There are also encountered in this area a very few cells approaching the type of the epithelioid cells of the bacillar tubercle. The larger necrotic focus found in the center of the right lobe likewise consists of cells in a state of complete coagulation necrosis and finely granular material. At the periphery of the mass there is a zone of cellular infiltration composed of small lymphoid cells, mixed with considerable numbers of ordinary polynuclears. Eosinophiles are not seen. In the interior of the necrotic mass there are found a number of reticula of typical fibrin which gives Weigert's reaction. It is in connection with this fibrin and in its neighborhood that great numbers of shell-like plague bacilli are encountered. No plague bacilli are found in other parts of the hepatic sections. Neither in the small tubercle nor in the larger necrotic focus could any

tubercle bacilli be demonstrated. In the lungs the vessels are dilated and the alveoli are mostly open, some of them containing desquamated epithelia, others fairly numerous red blood corpuscles, and still others a hyaline or finely granular material, evidently the product of an oedematous fluid, coagulated by the fixing and hardening liquid. No plague bacilli are found in the pulmonary sections. The gastric vessels are dilated and greatly engorged. Much blood extravasation has taken place from the interglandular capillaries. The petechiæ and ecchymoses are in the outermost layer of the mucosa and often separated from the surface only by a thin remnant of tissue. The other zone of the mucosa towards the free surface is necrotic and its cells are swollen and have lost their nuclei. Numerous plasma mast cells are seen in the submucosa. Plague bacilli do not appear in the areas of blood extravasation, nor anywhere else in the stomach wall.

CASE NO. 14. RIGHT CERVICAL BUBO WITH SECONDARY PLAGUE  
SEPTICO-PYEMIA.

[Necropsy Protocol No. 889. E. J., Filipino, male, 63 years old, from No. 142 Caballeros Street, San Nicolas District. Died February 18, 1904, at 1 o'clock p. m. Sick five days; cause of death unknown. Post-mortem examination made February 19 at 8.45 o'clock a. m., about twenty hours after death.]

The body of a native well advanced in years; hair gray. Post-mortem rigidity still fairly well marked, but beginning to disappear. The post-mortem lividity is pronounced on dependent parts and spreads toward the sides and interior surfaces of the body. The integument shows no injuries or sores. There are no buboes externally visible in the inguinal, cervical, or any other region. The abdomen is slightly distended. On section some dark, fluid blood escapes from the severed veins. The peritoneal and pleural cavities contain a small amount of serous fluid, the serous membranes are somewhat dull and their vessels markedly injected. The pericardium contains a small amount of clear fluid. The heart muscle is soft and flabby; the left ventricle is moderately contracted, and the right one dilated. The external surface shows a number of small irregularly distributed subepicardial petechiæ. The myocardium is pinkish-yellow. The valves are normal. The arch of the aorta is atheromatous. Lungs: Both apices are adherent, the adhesions being firm and fibrous. Externally the lungs are dark purplish-blue in color; on section they are dark purplish-brown. They are rich in dark, fluid blood, but do not contain much



air. The bronchi show a swollen and congested mucosa, and contain a moderate amount of viscid mucus. The mucosa of the trachea and larynx is congested, particularly that of the epiglottis. The spleen is small and its capsule slightly wrinkled and rather soft in consistency. On section the trabeculae are well marked, the Malpighian bodies are indistinguishable and the soft pulp soft and dark brownish-red. The kidneys are normal in size; their capsules are smooth, rather dull, and purplish-blue. On section the surface is grayish-white, and the vessels considerably injected and prominent. The mucosa of the pelvis is smooth and hyperemic. Liver: The capsule is smooth and purplish-blue with some grayish-white. On section the veins discharge a good deal of blood; the surface is smooth and dull brownish-yellow. Here and there a pale gray, soft necrotic focus of small size is seen. The gall bladder and ducts are normal. The gastric and intestinal mucosa is hyperemic, the former showing a moderate number of small hemorrhagic spots. The lymph glands in general are not much changed, except the right superficial cervical glands, which are swollen, soft, cedematous, and highly congested, but not diffusely hemorrhagic.

*Anatomical diagnosis.*—Congestion and œdema of the lungs; congestion and parenchymatous degeneration of the kidneys; subserous and submucous hemorrhages; right cervical bubo. Plague.

Smears from the cervical glands of the right side show numerous plague bacilli as well as numerous delicate, small streptococci. Culture tubes inoculated from the cervical glands and from the spleen developed a typical plague growth. No streptococci were found in the cultures.

*Microscopic examinations.*—The capsule of the cervical glands is thickened, and the connective tissue at the hilum much increased. The vessels of the capsule and the hilum are dilated and much congested. The entire substance of the glands is traversed by dilated, densely filled vessels; the differentiation into follicles is almost completely lost, the medullary cords are no longer distinguishable. The peripheral lymph sinus is dilated and contains a number of mononuclear cells and a good deal of granular material. The blood vessels, though dilated and much congested, show no marked changes in their walls, except some thickening of the adventitia; they do not contain any fibrin but are densely crowded with

erythrocytes, and show an increased number of leucocytes. The cells of the lymphatic tissue proper consist of small mononuclears of the ordinary type and a considerable number of plasma mast cells. Eosinophiles are not seen. Great numbers of plague bacilli are found in the lymph sinus, in the other distinct lymph channels, vessels, and clefts and all over the gland substance. The interior of the most of the blood vessels generally is free from bacilli, although some of the vascular lumina show these organisms in considerable numbers. Gram's stain shows no streptococci in this gland, though smears made from the cervical glands at the post-mortem examination contain typical streptococci. Spleen: The trabeculæ and the walls of the splenic arteries are thickened; some of the Malpighian corpuscles are still recognizable, although most of them can no longer be distinguished, even those which are preserved being quite small. In general, corpuscles and pulp form one almost structureless mass consisting of a large number of red blood corpuscles and mono- and polynuclear cells. The original pulp spaces can no longer be outlined, and all of the splenic tissue is profusely infiltrated with plague bacilli; however, these are not found in large solid masses, as in the lymph glands, but in small groups. The kidneys show profound parenchymatous degeneration. The lining epithelia of the convoluted tubules have generally lost their nuclei; the cells as a whole are much swollen and indistinct in outline; and the tubular lumina are more or less obliterated by granular material. The straight tubules show the same changes, though to a much less degree. The glomeruli do not show such profound changes, and are fairly normal in appearance, though quite a number of plague bacilli are found in some of them. However, these organisms are located, as it appears, not in the glomerular capillaries but between the loops of the tufts. The lymph clefts between the tubules likewise contain plague bacilli, but in moderate numbers only. The liver shows some very small interlobular inflammatory foci composed of small round cells, and here and there some increase in fibrous connective tissue around the interlobular vessels and bile ducts. The parenchyma cells are finely vacuolated. The capillaries are rather distended but not well filled with blood. In general the hepatic capillaries show very few plague bacilli, except in some places—i. e., those corresponding to the necrotic foci seen at the autopsy, where we find enormous sausage-like masses of these organisms. They are located

in the capillary lumen, none being seen inside the cells. The parenchyma cells in the neighborhood of these bacterial emboli show evidence of necrobiosis (poorly stained nuclei, etc.). The pulmonary tissue exhibits alveoli partly filled with desquamated, pigment-containing alveolar epithelia, and granular material, while here and there may be seen an air space almost completely filled with blood. The interalveolar capillaries and the other pulmonary blood vessels are much congested and densely filled with blood. Quite a few plague bacilli are found in the interalveolar connective tissue. It appears that these organisms are located inside the epithelial cells lining the lymph clefts, some also being found inside the alveolar epithelia. None are found in the pulmonary blood vessels. The alveoli show the presence of a small number of large, slender bacilli, which, like the organisms of plague, are decolorized by Gram's method.

#### CASE No. 15. RIGHT AXILLARY BUBO.

[Necropsy Protocol No. 973. F. A., Filipino, male, age 28 years, from 661 Calle Billbid, Santa Cruz; died May 9, 1904, at 11 o'clock p. m. Post-mortem examination made fifteen hours after death.]

The body of a strong, well-developed man between 25 and 30 years of age. Nutrition is good. Post-mortem rigidity is marked; post-mortem lividity is well developed. Near the right nipple there are seen two dried-up vesicles, which are completely collapsed and covered with dry epidermal scales. Otherwise there are no open wounds on the body. The right axillary lymphatics form a flat doughy mass of the size of the palm of the hand. The swelling in the right axillary space is not well defined but gradually shades off into the surrounding tissue; the skin overlying this region is very cyanotic. On being cut the mass is found to be very œdematous and it first discharges a blood-tinged serum and then a bloody fluid. No individual glands can be mapped out, but everything is completely infiltrated by a hemorrhagic exudate. The latter is continued into the deep fascia of the thorax and the pectoral muscles, finally reaching the intercostal muscles and penetrating into the thorax. The inguinal, cervical, and cubital glands are all to a certain extent palpable, and, when dissected out, are found to be somewhat enlarged, softened, and congested. On opening the body cavities the serous membranes are seen to be congested and rather dull. The serous fluid in the abdominal and thoracic cavities is not increased. The right lung has formed a few slight

adhesions. On the right side there is found an area of subpleural hemorrhage, which forms a direct continuation of the ones radiating from the axillary bubo. The lungs are in general normal in form, fairly well inflated, and purplish-blue in color, with a few small subpleural hemorrhages. The pulmonary tissues are congested and cedematous. The mucous membrane of the trachea, the bronchi, and the larynx is somewhat swollen and highly congested. The heart is normal in size. The coronary vessels and their branches are much engorged. A few subepicardial hemorrhages are found on the anterior surface. The myocardium is rather soft and flabby and pinkish-yellow in color. Otherwise the heart is normal. The spleen is twice its normal size, quite soft, steel-gray externally, and reddish-brown on section. The pulp is quite soft. The trabeculae are well marked, the Malpighian bodies less so. The liver is normal in size, though somewhat increased in consistency. It is purplish-blue in color with some grayish-white mottlings. On section it is found to be much congested. The gall bladder is normal, containing a large amount of yellow, thin bile. The kidneys are normal in size, smooth, bluish-purple externally, and yellowish-pink on the cut surface. The pelves are much injected, that of the left kidney containing a small amount of extravasated blood. The adrenals are normal in size, of fair consistency, and brownish-yellow in color. The mucosa of the stomach shows numerous small hemorrhagic spots, which are also seen in moderate numbers in the duodenal mucosa. The lymphatics of both the large and the small intestine are somewhat swollen.

*Anatomic diagnosis.*—Congestion and edema of the lungs; parenchymatous degeneration of the kidneys; right axillary hemorrhagic bubo; general swelling, hypertrophy, and congestion of the lymph glands. Bubonic plague.

Smears made from the different organs show plague bacilli, which are present in considerable numbers, together with some diplococci in those from the axillary hemorrhagic bubo, and in fair numbers in the left inguinal glands and in the liver, while in the spleen they are plentiful. The cultures developed typical plague bacilli, but all were contaminated.

*Microscopic examination.*—The right axillary glands show an almost complete necrosis with a loss of all the finer details of structure and an intense hemorrhagic infiltration, which extends into the surrounding tissue. A considerable number of very poorly

staining plague bacilli are seen in the sections. The inguinal glands exhibit an increase of connective tissue at the hilus, great oedema, general vascular dilatation, and engorgement with hyaline degeneration of the rarefied vessel walls. A moderate number of plague bacilli are present in the inguinal glands. In the spleen the Malpighian corpuscles are small and the pulp spaces are not very distinct, being crowded with many polynuclears. The erythrocytes are only moderately numerous. The lymphatic endothelia of the pulp spaces have proliferated to a moderate extent, some of them showing two or three nuclei. The splenic sections contain innumerable plague bacilli; however, they are not present in such solid zoogloal masses as are frequently seen in primary buboes, but in very dense groups consisting of many hundreds of bacilli, between which the tissue cells are only sparingly seen. This condition is most marked in the peripheral lymph sinus. In the pulp spaces the bacilli are less numerous, though present to a large extent. A great condensation of bacillar masses is also seen at the peripheries of some of the Malpighian corpuscles, while their interior is almost entirely free from microbic invasion. Phagocytic cells containing bacteria are not seen in the spleen. The kidneys show a most profound degree of cloudy swelling of the tubular epithelia, with the presence of much granular material and some hyaline casts. All the vessels are much dilated and engorged, particularly the glomerular capillaries. Here and there in the glomeruli an incomplete fibrin thrombosis is met with. Groups of plague bacilli are found in the glomerular and intertubular vessels, some of them amounting to fairly dense masses of bacteria. A very few isolated bacilli are seen here and there in the uriniferous tubules. The hepatic sections exhibit veins and capillaries much dilated and engorged with an increased number of leucocytes. The parenchyma cells are vacuolated and coarsely granular, their nuclei often being poorly stained and even lost. The capillaries show small, loose groups of plague bacilli, but nowhere a complete occlusion by dense bacillar masses, as seen in other cases of bubonic plague, with metastatic bacterial emboli of the liver. In the pulmonary sections the veins and the interalveolar capillaries are greatly dilated, and the latter here and there contain small, loose groups of plague bacilli. Very few single bacilli are seen in the alveoli. Here and there they are in contact with the wall, so that their derivation from the intracapillary groups is probable.

### GROUP III. PRIMARY BUBONIC PLAGUE WITH SECONDARY PLAGUE PNEUMONIA.

#### CASE NO. 16. AMBULATORY PLAGUE, OR PESTIS MINOR.

It has been known for many years, long before the specific bacillus had been discovered, that plague cases exist in which the symptoms are very mild and in which the patient may be free from any marked elevation of temperature. These have been called ambulatory plague or *pestis minor* and have quite properly been compared to typhus ambulatoria.

Griesinger, Liebermeister, Montague-Lubbock, Manson, Scheube, and others have called attention to the fact that such ambulatory cases, in spite of the mild character of their symptoms, are liable to sudden collapse and fatal termination. Manson (*Tropical Diseases*, 3d edition, London, 1903, p. 249) speaks of this type as abortive or larval plague, and states that certain epidemics are distinguished by a larger proportion of mild cases. "In such," he says, "buboes form and suppurate or resolve, the associated constitutional symptoms are comparatively mild or perhaps altogether wanting. In every epidemic there may be cases in which the patient is able to be about, having little, if any, fever, and apparently being little inconvenienced by the disease. Such cases, however, may collapse suddenly."

However, there is very little to be found in literature showing that a more careful investigation of this type of cases has been made. So scanty is our knowledge that the extensive report of the Indian Plague Commission has no more to say about the pathology of *pestis minor* than the following (Vol. V, p. 432): "Death from *pestis minor* probably never occurs, but, at any rate, no description of the pathology of plague deals with this type."

The case to be reported as an example of ambulatory plague demonstrates that the term "*pestis minor*" is a misnomer, when applied to such "walking-plague patients" as die suddenly. In our case the necropsy and the microscopic examinations furnished evidence sufficient to account for the unexpected death in the absence of any marked previous subjective symptoms of ill health. The history and the findings in this case, which is somewhat complicated by a simultaneous, evidently very recent, tuberculosis of the lungs, were as follows:

The death of a Filipino lad, 17 years old, was reported to the Santa Cruz board of health station, Manila, P. I., on February 27, 1904, at 11 o'clock a. m. The body of the deceased was found in a dimly lighted loft in the corner of a lower unpaved room, adjoining a soda-water factory at No. 185 Calle Misericordia. On

examination nothing worthy of note was seen, except enlargement of the glands in the inguinal region and Scarpa's triangle on both sides, as well as a chronic skin affection of both legs. The position of the body had been changed since death. The boy had been employed for general purposes about the place for from four to five months, during which time he appeared to be in good health, except that for some weeks before his death his face was rather pale, and he did not sleep very well. He spent the evening of February 26 playing in the street with other boys until 11 o'clock, when he went to bed. About 12 o'clock he awoke, complaining of pain in the chest and difficulty in breathing. His condition soon became alarming, and a native physician was sent for, who was unable to do anything for him. At 2 o'clock he was dead. (History furnished by district medical inspector, Dr. Terry, of the Board of Health.)

CASE No. 16. AMBULATORY PLAGUE. TERMINATING BY EMBOLISM OF THE PULMONARY ARTERY.

[Necropsy Protocol No. 901.]

Post-mortem examination made on February 27, 1904, at 3 o'clock p. m. The body of a Filipino boy, about 17 to 18 years of age and well developed. Post-mortem rigidity strongly marked; post-mortem lividity prominent on dependent parts and extending over the sides of the trunk and neck as well as over the anterior surface of the latter. A greenish-brown, foamy, ill-smelling fluid oozes from the anterior nares. The anterior surface of the lower extremities, from the ankles upward to about midway between the knees and Pupart's ligaments, is covered with a vesiculo-pustular eruption. The lowermost portions of this eruption consists of shallow ulcerations covered with brownish, bloody scabs. The skin lesions higher upon the thigh are still purely vesicular and the collapsed vesicles are covered with epidermal scales. The chain of lymph nodes below Pupart's ligaments on both sides is swollen, the most marked swelling being found in the lowermost glands on each side. The swollen region is soft and doughy. However, no fluctuations are noticeable. On incision of the skin the superficial veins discharge a rather small amount of dark, fluid blood. The pericardium is smooth and normal, and contains a small amount of clear, straw-colored fluid. The visceral layer of the pericardium shows dilated and congested veins. On the posterior

surface, over the left auriculo-ventricular zone two or three dozen hemorrhagic areas are seen, varying in size from a pin-head to a millet seed. Otherwise the visceral pericardium is normal. Heart: The myocardium is fairly firm and somewhat pale. The left ventricle is contracted, and the right one dilated. The latter contains a rather firm, though somewhat gelatinous, reddish-gray coagulum, which does not completely fill the ventricular cavity. The coagulum is continued into the pulmonary artery, which it completely fills. Here it is firmer in consistency and decidedly more grayish in color. These variations from the consistency and color of the clot in the heart became greater the farther the distance from the entrance of the pulmonary artery to the interior of the ventricle. The thrombus extends into the main branches of the pulmonary artery, from where it can be followed into the lower, secondary branch of the right side, and it is then lost in the highly congested lower lobe of the right lung. A distinctly hardened infarcted area can not be found. The blood in the left ventricle and auricle is fluid and of a dark purple color. The lungs are quite firmly adherent to the parietal pleura. The lower lobe of the right lung is particularly firmly adherent to the diaphragm. The partly obliterated pleural sacs contain a small amount of slightly turbid, yellowish fluid. The upper lobes are dark grayish-pink and contain a considerable amount of air; the lower lobes, particularly the right one, are dark purplish-blue and contain very little air. On section the lower lobes are found to be quite cedematous and filled with a very dark, purplish, fluid blood, which oozes out freely from the larger and smaller vessels. The right lower lobe on the cut surface shows some small, grayish-white dots. The bronchi contain a small amount of foamy, grayish-white fluid. Their mucous membranes are injected and rather bright-red in color. The trachea and the larynx likewise show swollen, injected mucosa. The spleen is large and bluish-pink in color, its capsule smooth and shining. The cut surface is dark purplish-brown. The trabeculæ and the Malpighian corpuscles are distinct. The pulp is fairly firm in consistency. The kidneys are rather small and their surface smooth and of a dark grayish-pink color. The capsules peel off easily, and the denuded surfaces then show the small vessels to be much injected. They stand out plainly on a grayish-yellow background. On section the vasa recta and the glomeruli appear quite strongly injected and intensely scarlet.



The tubules are quite markedly yellowish-gray, the surface on the whole being rather dull. The pyramids are purplish. The mucous membrane of the pelves is smooth and somewhat congested. Liver: The capsule is smooth, shining, transparent, and pinkish-gray in color, some areas being decidedly mottled. The cut surface shows the center of the lobules to be grayish-white; they are distinct in outline. The surface as a whole is dull. The veins contain much dark, fluid blood. The gall bladder contains some turbid, greenish-yellow bile, its mucous membrane being smooth. There are no stones; the ducts are normal. The stomach and intestines appear fairly normal. The suprarenals and the pancreas are normal. The inguinal glands on both sides are enlarged, swollen, soft, and rather bluish-pink in color. On section they show injected vessels, which stand out prominently on a grayish-yellow background. The substance of the glands is soft. No abscess formation has occurred. An abundant, grayish-white fluid can be scraped from the cut surface. The lower glands of the chains on each side are the largest, showing a central softening quite markedly. There is, however, no abscess formation. These glands are equal in size on both sides and measure 4.8 by 3.7 by 1.7 centimeters. The mesenteric, the cervical, and the other glands examined are all moderately enlarged and more or less congested. Marked congestion exists in the bronchial glands.

*Anatomical diagnosis.*—Congestion and œdema of the lungs; parenchymatous degeneration of the kidneys; embolism of the pulmonary artery; inguinal buboes. Plague.

Smears were made during the post-mortem examination from the liver, the spleen, and the glands. In the smears from the spleen and the glands only a very small number of bacilli are found. They are more numerous in those from the liver. Some of the bacilli found in the latter are quite typical in appearance, showing polar staining and rounded ends. Other bacilli are swollen, somewhat irregular, and approaching the type of the involution forms seen on artificial media. Still others are small and look decidedly like diplococci. Others form small chains, the individual members of which appear to be in a state of partial dissolution. The cultures inoculated from the organs developed typical plague bacilli.

*Microscopic examination.*—Liver: The liver shows extensive interlobular, inflammatory foci, formed by a cellular exudate.

The infiltrating cells are found around the interlobular arteries, veins, and small bile ducts. The small interlobular vessels show a marked thickening of the adventitia, and most of the lumina are found to be surrounded by a number of concentric rings, composed of delicate connective tissue fibers. Occasionally there is found a small vessel entirely occluded by an obliterating proliferation of the lining endothelium. The cellular exudate of the inflammatory foci consists of lymphoid cells and a high percentage of eosinophilic polynuclears. In some places the latter form one-fourth to one-fifth of the total number of infiltrating cells. Plasma cells are very sparingly represented. While this description conforms in general to most of the inflammatory foci in the liver, other areas present decidedly varied appearances. In these the foci, which are more or less nearly circular, clearly show a center consisting of epithelioid cells with a vesicular nucleus and a large protoplasmic body. Multinuclear giant cells are found in some of the nodules. The histology of these round or oval nodules is clearly that of the bacillar tubercle. The nodules also show a fine, concentrically arranged, fibrillar network of connective tissue fibers. Regressive changes are not seen. There is no caseation, nor does Weigert's stain show any fibrin. The histology of the small tubercles in the liver, and it may here be added that of the similar structures found in the lungs, is identical with what has recently again been described by Baumgarten as being the structure of the tubercle experimentally produced and about two or three weeks old, which has not yet undergone any regressive changes, but in which the appearance of the first giant cells indicates that the proliferation of the tubercle bacillus, as well as that of the inflammatory cells, has come to a standstill. Baumgarten also describes the occlusion of small vessels by endothelial proliferation brought about by the presence of the tubercle bacillus. The nodules in the liver as well as those in the lungs contain an element which is foreign to the typical uncomplicated tubercle, namely, numerous eosinophilic polynuclears. It is impossible to prove the presence of tubercle bacilli, but the tubercles are found to be infected with the organisms of plague. The latter are seen here and there in both types of inflammatory foci, in those which simply show the structure of an ordinary inflammatory area, and in those possessing the features of a bacillar tubercle. The parenchyma cells of the liver exhibit a moderate degree of fatty degeneration. The capil-

laries are well filled with blood. Lungs: Section from the right lower lobe show a great engorgement of the interalveolar capillaries; in fact, all the blood vessels are highly congested. The alveoli present a varying picture; some of them are open, having contained air only, and others are filled with extravasated blood, which does not show any degenerative changes. Desquamated alveolar epithelia, containing hematoidin granules, are seen occasionally. The unchanged character of the blood, the small amount of pigment-containing alveolar epithelia, and the absence of areas of coagulation necrosis, show that the blood extravasation must be of comparatively recent in date. Quite a few of the air spaces are filled with homogeneous coagulated material, which stains deeply with eosin. Other alveoli contain a lighter staining material. Neither the homogeneous nor the granular material takes Weigert's fibrin stain, nor do the capillaries contain any hyaline (fibrin) thrombi. Here and there is found a small solid nodule, hardly greater in size than the larger alveoli themselves. These nodules are composed of epithelioid and lymphoid cells and a considerable number of eosinophilic polynuclears. Multinuclear giant cells are likewise found in or near the center of some of the nodules. In fact, the latter are absolutely identical in their make-up with the tubercles which may be seen in sections of the hepatic tissue. Both in the pulmonary and in the hepatic tissue neighboring nodules are found, the peripheries of which are in contact with each other. However, the individual nodules have not become confluent and their outlines are well preserved. It is impossible to demonstrate tubercle bacilli in these nodules, but they show a small number of the bacilli of plague, found scattered between the cells. In properly stained sections it is seen that some of the alveoli contain enormous numbers of plague bacilli, such air spaces appearing almost filled with them. Small groups of scattered plague organisms can be found throughout the sections. Inguinal lymph nodes: The inguinal lymph nodes show numerous large, dilated vessels, replete with blood corpuscles. Around the larger vessels, particularly of the hilus vessels, there is a powerful development of the connective tissue. The general fibrillar connective tissue reticulum is everywhere much increased. The peripheral follicles generally show a well differentiated proliferation center. The peripheral lymph sinus and its branches are dilated. Eosinophilic polynuclears are found throughout the tissues, though nowhere in such large numbers

as in the lungs and liver. Bacilli are seen but sparingly in the sections. Kidneys: Sections of the renal tissues show practically normal glomeruli, moderate parenchymatous changes in the tubular epithelium, and highly congested vessels.

The noteworthy features of this case are its ambulatory nature, its sudden termination by embolism of the pulmonary artery, and its complication with what undoubtedly appears to be a very recent tuberculosis. According to Scheube tuberculosis is a very grave complication of plague; and Pearse likewise considers it a very unfavorable factor in this disease. It is very probable that in the case reported the plague virus first gained entrance through the skin lesions of the legs into the inguinal glands, where only a moderate multiplication occurred. The bacilli were then transported in the shape of a metastatic embolism into the lungs, from where the embolism grew until it obliterated the pulmonary artery. During the time these pathologic processes were going on, the symptoms were so mild that the plague-infected patient never stopped his regular work nor felt called upon to consult a physician.

#### **GROUP IV. PRIMARY UNCOMPLICATED PLAGUE PNEUMONIA.**

##### **CASE No. 17. PRIMARY UNCOMPLICATED PLAGUE PNEUMONIA.**

[Necropsy Protocol No. 970. A. Q., Chinese, male, 30 years old, a shopkeeper from No. 67 Tetuan, Santa Cruz. Sick six days; died May 18, 1904, at 10.30 p. m. Post-mortem examination made thirteen hours after death.]

The body of a well-developed Chinese about 30 years of age. Post-mortem rigidity moderately marked; post-mortem lividity well marked, extending to the anterior surfaces of the body. The skin as a whole is markedly cyanotic. The right axillary glands are slightly palpable; the other superficial ones are not. There are no injuries, wounds, or abrasions of the integument. On section, a moderate amount of dark, fluid blood escapes from the veins. The muscles are fairly moist and of a dark red (smoked meat) color. The serous membranes are injected and rather dull. The pericardium is much injected and contains a slightly increased amount of a yellowish somewhat turbid fluid. The heart is normal in size, the left ventricle contracted, and the right one dilated. At the sulcus a number of subepicardial hemorrhages are seen, the largest of which is about 0.5 to 0.6 centimeter in diameter. Both sides contain gelatinous post-mortem clots. The valves, the

endocardium, etc., are normal. The myocardium is of good consistency and reddish-pink, with a slight shade of yellow. The aorta and the coronaries are normal. Lungs: A few adhesions are found at the upper lobe of the right lung. The left pleural cavity contains an increased amount of fluid. The pleural surfaces are deep purplish-blue, particularly on the right side, the left side showing some admixture with grayish-white. On section, the right lung is found to be much congested and highly œdematous. The bronchi contain a fair amount of slightly blood-stained, frothy mucus, the alveoli only a small amount of air. The left lung is quite heavy, the lower lobe being entirely consolidated, and the greater portion of the upper one is in the same state. On section the consolidated pulmonary tissue is light brownish-gray. The cut surface is quite granular, and the juice which can be scraped off is bloody-grayish-yellow and quite turbid and opaque. In the upper lobe the consolidated area gradually shades off into the surrounding tissue and is not sharply defined. On a closer inspection both of the consolidated areas, in the upper lobes as well as in the lower show foci, varying in size from a pea to a hazelnut, grayish-yellowish-red in appearance, and surrounded by much congested, dark red areas. The bronchial glands are swollen, and very soft and dark, their contents being changed into an almost black, cheesy mass. The mucosa of the bronchi, the trachea, and the larynx are swollen and congested. The spleen is normal in size and flabby, with a wrinkled surface somewhat bluish-gray in color. On section the pulp is soft and protrudes over the surface, being dark reddish-brown in color. The Malpighian bodies and the trabeculæ are not very distinct. The kidneys are normal in size and their surfaces purplish-pink in color. On section, the vessels are much engorged, the tubules grayish-white, and the surface dull. The mucosa of the pelvis is much injected. The suprarenals are swollen, softened, and brownish-purple in color. The liver is large and of increased consistency, its surface being purplish-blue with a great deal of grayish-white in some places. The cut surface is decidedly pinkish-yellow and as a whole dull. The vessels are much engorged. Stomach: The serosa shows a very few small hemorrhagic spots; the mucosa contains very numerous petechiæ and ecchymotic areas. The duodenal mucosa likewise shows some hemorrhagic spots. The lymphatics of the small intestine are somewhat swollen. The mediastinal, the mesen-

teric, the retroperitoneal, and the other superficial glands are all moderately swollen and congested. On section their vessels are found markedly engorged and their substance somewhat softened. The most pronounced enlargement is found in the axillary glands of both sides. Smears from the consolidated areas of the left lung show innumerable typical plague bacilli; those from the glands and blood only a few.

*Anatomical diagnosis.*—Parenchymatous degeneration of the kidneys; fatty and parenchymatous degeneration of the liver; multiple subserous and submucous hemorrhages; lobular pneumonia of the right lung. Plague pneumonia.

Cultures inoculated from the consolidated areas of the right lung developed a typical growth.

*Microscopic examination.*—Lungs: The alveolar spaces in the consolidated area are all more or less completely occluded. The distended air sacs, filled with a completely granular detritus, alternate in an irregular manner with the alveoli which are filled with a cellular exudate. The interalveolar septa are generally markedly broadened, however, this is not due to a marked increase in the cellular elements but to an œdema and hydropic swelling of the fibers and cells forming the interalveolar septa. The capillaries are greatly engorged and the walls of the veins are œdematous, loose, and frequently in a state of hyaline degeneration. Fibrin in finer or coarser threads is quite extensively seen, both in the interior of the alveoli and in the interalveolar tissue. The cellular exudate in the air spaces consist mostly of polynuclears with some mononuclears and desquamated epithelial cells. Erythrocytes are present everywhere, but in moderate numbers. Plague bacilli are found throughout the consolidated area, but not in very dense zooglœal masses, though in great numbers in some places. In the renal tissue the most profound changes are cloudy swelling and fatty degeneration of the epithelia lining the uriniferous tubules. The interstitial tissue is quite œdematous, and the interstitial capillaries are filled ad maximum. The glomerular vessels are likewise engorged, but otherwise do not show any profound changes. No plague bacilli are found in the renal tissue. The liver shows small, interlobular, inflammatory foci, composed mostly of mononuclear and embryonal connective tissue cells and a few polynuclears. However, these foci are quite small. The parenchyma cells show fine as well as coarse vacuolation. The interlobular capillaries contain a good

deal of blood. The spleen shows no marked histologic changes, and only a very few bacilli are seen after a prolonged search. Several lymph glands show marked dilatation and engorgement of their blood vessels as well as some œdema; otherwise they are fairly normal. The stomach exhibits greatly dilated vessels and capillary hemorrhages between the glands and upon the surface of the mucosa. No plague bacilli are found in the gastric areas of blood extravasation. In fact, none of the organs except the lungs contain any large number of these organisms. Outside the pulmonary tissue they are practically not found at all. The necropsy of this case shows it to be a pure plague pneumonia, without a general septic or septicopyemic dissemination of the bacilli.

#### CASE NO. 18. PRIMARY UNCOMPLICATED PLAGUE PNEUMONIA.

[Necropsy Protocol No. 971. C. C., Chinese, male, 27 years old, from No. 67 Tetuan, Santa Cruz. Sick six days; died May 18, 1904. Post-mortem examination fourteen hours after death.]

The body of a slender Chinese from 25 to 30 years of age. Post-mortem rigidity well marked; post-mortem lividity moderate. The surface is slightly cyanotic. There are no external wounds or ulcerations. None of the superficial lymphatics are palpable. On section the veins discharge a good deal of dark, fluid blood. The muscles are fairly moist and reddish-brown. The serous membranes are injected and dull. The pericardium is much congested, but the pericardial fluid is normal. The heart is normal in size, the left ventricle well contracted and the right one dilated. The anterior surface of the left ventricle, the apex on all sides, and the sulcus show numerous small subepicardial hemorrhages. Both sides contain gelatinous coagula. The myocardium is rather soft, pale, and reddish-pink. Otherwise the heart is normal. The aorta and coronaries are normal. Lungs: The entire anterior and a part of the posterior surface of the lower lobe of the left lung is completely adherent to the pleura costalis. After the removal of the left lung it is found that the pleura pulmonalis of the lower lobe is thickened, yellowish, and covered with a thin fibrinous deposit. Both pleural sacs contain a slightly increased amount of fluid, on the left side this is turbid and contains some fibrinous flocculi. Externally the left lung is purplish-blue and the right one scarlet-pink. On section it is found that the lower lobe of the left lung contains a central area of pneumonic consolidation. In front this

extends as far as the pleura, and posteriorly and below it reaches to within about one centimeter of the pleural surface; but above there are still several centimeters of pulmonary tissue not yet in a state of consolidation. In the consolidated area the tissue is dark brownish-gray with lighter grayish-yellow spots. The cut surface is granular. The juice which is scraped off is turbid, grayish-white, creamy, and purulent. The area of consolidation is sharply defined from the rest of the pulmonary tissue, which is very much congested, dark brownish-red in color, and very cedematous, containing very little air. The upper lobe of the left side is congested and cedematous and contains much dark, fluid blood. The right side on section is found to be moderately congested and to contain quite a fair amount of air. The bronchial mucosa and that of the trachea and larynx are congested. The bronchial glands are swollen, softened, and dark purplish. The spleen is small and flabby and its surfaces wrinkled and bluish-gray. On section the dark-brown pulp is found to be softened, the trabeculae visible, and the Malpighian corpuscles swollen. Kidneys are greatly congested. On section the vessels stand out very prominently on a very markedly grayish-yellow background. The surface is very dull. Liver: The surface is bluish-purplish-pink with gray mottling. The consistency is moderately increased. The cut surface is yellowish-brown and dull. The vessels are much engorged and the lobules enlarged. The gall bladder and ducts are normal. The gastric and duodenal mucosa shows numerous petechiae. The petechiae are so numerous and crowded in the mucosa of the stomach at the fundus that they have become more or less confluent at their margins. None of the superficial or deeper lymph glands, excepting the bronchial ones, show any marked changes.

Smears from the consolidated area of the lung show innumerable typical plague bacilli; others only a very few.

*Anatomic diagnosis.*—Parenchymatous degeneration of the kidneys and liver; multiple subserous and submucous hemorrhages; pneumonia; acute adhesive fibrinous pleurisy. Plague.

*Microscopic examination.*—Sections from the consolidated area of the lung show alveoli filled with mononuclear and polynuclear leucocytes, erythrocytes, and alveolar epithelia. The polynuclear leucocytes predominate considerably. Some of the air spaces show a coarse network of fibrin, though such places are not numerous. However, fibrin is found very extensively in the interalveolar capil-



laries and in some of the smaller pulmonary veins; it is present both in the shape of a reticulum and in that of tubular or solid thrombi. Here and there an extension of the intravascular fibrin into the vessel wall and into the perivascular tissue is encountered. The intervalveolar septa in this case, unlike those in the preceding one, are not at all widened but rather delicate, excepting the space occupied by the distended capillaries. Bacilli are found extensively throughout the sections; here and there in a dense clump located in an alveolus and in other places distributed in such a way that it may be said that the cells of the exudate are embedded in a loose reticular matrix consisting of plague bacilli. In the renal tissue the tubular epithelium shows cloudy swelling, granular and fatty degeneration, and a loss of nuclei. Many of the tubules are collapsed and the interlobular connective tissue is oedematous. The capillaries, including those of the glomeruli, are congested, and a few microscopic areas of blood extravasation are found near the capsule. Sections of the liver show cloudy swelling and fatty degeneration of the parenchyma cells and great congestion of the capillaries and veins. However, there are no interstitial changes. The lymph glands exhibit engorgement of the blood vessels and lymph channels, some slight oedema, possibly some increase in fibrous connective tissue, and the presence of quite a number of plasma mast cells. Otherwise no changes have occurred. The vessels of the gastric and duodenal mucosa are greatly engorged, and some blood extravasation has taken place into the mucosa upon its surface. No plague bacilli are found in these small hemorrhagic areas; in fact, practically none of these organisms are found outside the pulmonary tissue. (The tissue from the spleen of this case had been lost.)

#### **GROUP V. PRIMARY PLAGUE PNEUMONIA WITH SECONDARY PLAGUE SEPTICO-PYEMIA.**

##### **CASE NO. 19. PRIMARY PLAGUE PNEUMONIA WITH SECONDARY SEPTICO-PYEMIA.**

[Necropsy Protocol No. 962. F. S., Filipina, female, 30 years old, from No. 148 Calle Anda, Intramuros, Manila. Died May 7, 1904, at 5.30 p. m. Cause of death unknown. Plague suspected. Post-mortem examination made sixteen hours after death.]

The body of a fat, stout woman, probably 40 years old. Post-mortem rigidity moderate; lividity well marked. The posterior surface and the sides of the trunk, as well as the extremities, show

numerous small petechiæ and ecchymoses, varying in size from one to several millimeters. The surface as a whole is cyanotic. On section the superficial veins discharge a good deal of dark, fluid blood. The serous membranes are highly injected and somewhat dull. The pericardium contains the usual amount of fluid, which is turbid and rather dark yellowish. The heart is somewhat enlarged, soft, and flabby. The left ventricle is very moderately contracted and the right one dilated, both of them containing clotted blood. The auriculo-ventricular openings are somewhat increased in size. The myocardium is soft and flabby, of a pinkish-yellow color, and easily torn. Otherwise the heart is normal. The lungs are adherent; the adhesions are easily broken up and are most marked on both the lower lobes and at the right apex. Both pleural cavities contain an increased amount of fluid of a turbid, slightly blood-stained character. The surfaces of both lungs are highly congested. The lower lobes particularly present numerous sub-pleural, hemorrhagic areas of an almost black purplish-blue color. Alternating with these are places where the surface is more grayish-pink. The hemorrhagic areas protrude somewhat over the general surface, so that the latter is somewhat uneven. On section the pulmonary tissue is found to be much congested with dark, fluid blood in some parts of the lower lobes this amounts almost to complete red hepatization. Inside these very much congested areas are seen spots of the size of a pea or smaller, which are grayish-red or more decidedly grayish-white. The lower lobes contain very little air, the upper ones a larger amount. The bronchial glands are not much swollen, though greatly congested, softened, and purplish-black in color, being somewhat hemorrhagic on section. The mucosa of the bronchi, the trachea, and the larynx is swollen and highly congested. The spleen is enlarged to about twice its normal size; its surface is bluish-purple and its capsule smooth and not very transparent. The cut surface is reddish-brown, uneven and granular, and the pulp protrudes. The trabeculæ are distinct; the Malpighian bodies are not. The kidneys are soft and almost gelatinous, their external surfaces being smooth, much congested, and deep purplish-blue. The capsules are transparent and peel off easily. On the cut surface the vessels appear highly engorged, the glomeruli stand out as deeply injected points, the tubules are grayish-white, and the surface as a whole is quite dull. The pyramids are much injected. The mucosa of the pelves is congested.

The suprarenals are swollen, soft, and dark brownish-yellow in color. The liver is large, of a somewhat increased consistency, and elastic. Its capsule is shining and transparent. The general color is pinkish-purple, but the areas of this hue alternate with places of a grayish-yellowish-pinkish color. On section the organ is found to be much congested. The hepatic veins discharge much dark, fluid blood. The surface is of a deep yellowish-brown and is quite dull. The acini are enlarged and the boundaries are not very distinct. Here and there a grayish-white point is seen on the cut surface. The gall bladder is distended, its walls œdematous, and its mucosa swollen. The bile is viscid and dark greenish-yellow. The ducts are open. The serosa stomach and the intestines is much injected and rather dull. The mucosa of the stomach and the duodenum shows numerous small, hemorrhagic areas. The pancreas is normal. The uterus is markedly enlarged and rather soft. Its mucosa is softened, swollen, and hemorrhagic. The cavity, however, contains no free blood. The serosa of the uterus as well as of the appendages is much congested. The uterine muscularis is of good, firm consistency. The left ovary is enlarged to the size of a large walnut, nearly perfectly spherical, microcystic, and of a deep black-bluish-purple color. The right one is small, firm, and less congested. No fresh corpus luteum is present. The inguinal and cervical glands are slightly enlarged and moderately congested but not softened. The internal lymphatic glands, such as the mesenteric, the retroperitoneal, the iliac, and the mediastinal, are all very moderately enlarged and markedly congested, but neither markedly softened nor hemorrhagic.

Smears prepared from the different organs show the following: Lungs: Very many typical plague bacilli, also a number of very small diplococci. Spleen: A moderate number of plague bacilli. Liver: Quite a few bacilli. Heart's blood: Quite a few plague bacilli and some small cocci. Kidneys: Numerous plague bacilli.

*Anatomical diagnosis.*—Lobular pneumonic foci; congestion and beginning diffuse red hepatization of both lower lobes; general congestion of the lungs; subpleural hemorrhages; congestion and parenchymatous degeneration of the liver and kidneys; submucous hemorrhages in the gastric and intestinal mucosa; hemorrhagic endometritis; microcystic degeneration and congestion of the left ovary. Plague pneumonia and septicæmia.

*Microscopic examination.*—Lungs: Sections from the most congested portions of the lower lobes show all the blood vessels, including the interalveolar capillaries, to be engorged *ad maximum*. Numbers of air spaces are filled with a granular detritus including desquamated cells, some white and a few red corpuscles. Mixed with these elements are a moderate number of typical plague bacilli, which in some of the alveoli are present to a considerable extent. The majority of them are found in close proximity to the inner lining of the alveolus and not free in the center of the air space. Alveoli completely filled with innumerable plague bacilli are also seen. In such masses of bacteria one occasionally encounters a vessel broken into by these organisms; this observation refers alike to the capillaries, the veins, and the arteries. On the other hand, a few interalveolar capillaries are found to be completely thrombosed with densely packed plague bacilli. Alternating with alveoli, more or less completely filled, are air spaces which are open and even emphysematous, the interalveolar space having occasionally been ruptured. No fibrin is found in any of the alveoli. Kidneys: The most striking histologic change in the kidneys are metastatic emboli in the glomerular capillaries, completely filling some of the loops of the tufts. However, such emboli are found in a limited number of glomeruli only; nor are any tufts seen where all the capillaries are obliterated. The embolic closure is generally confined to one lobe of a glomerulus. Sometimes the embolic bacterial mass extends into the afferent or efferent vessel (it is impossible to decide which of the two is affected). The neighborhood of such thrombosed vessels shows small microscopic areas of blood extravasation, in which few bacilli are found. All the renal vessels are much engorged, particularly the small vessels, and the interstitial tissue is quite oedematous. Small microscopic areas of blood extravasation are encountered all over the sections. A few bacilli are often seen in such areas as well as in the tubules, the lymph clefts, and even occasionally in the small arteries and veins. The tubular epithelium shows profound cloud swelling and fatty degeneration. The interlobular capillaries of the liver exhibit the same metastatic emboli, composed of dense masses of plague bacilli, such as have been described above for the renal tissue. However, these bacterial thrombi are not very numerous, and in general the liver capillaries are free from bacteria. On the other hand, a small number of bacilli were seen in one interlobular vein. The liver parenchyma

cells show marked fatty degeneration. In the spleen the Malpighian bodies and the pulp spaces are not well marked, and the latter are densely filled. The proportion of leucocytes is increased. The pulp spaces here and there show numbers of bacilli in fairly dense groups; but they are not nearly as crowded in the spleen as in the kidneys and liver. The gastric mucosa shows degenerative changes in the glandular cells, in most of which the nucleus stains poorly or not at all. Plague bacilli are found here and there in the loose connective tissue of the mucosa. The interlobular capillaries are enormously dilated, and blood is extravasated into the interglandular tissue and upon the free surface of the mucosa. Few plague bacilli are found in the œdematous and hemorrhagic interglandular tissue and in the areas of blood extravasation upon the mucosa. However, in general, the blood vessels do not contain any plague bacilli. The uterine mucosa is quite œdematous and its vessels much congested. Otherwise the uterus does not show any marked changes.

A consideration of the morbid anatomy and of the histopathology of this case shows that we are dealing with a primary plague pneumonia, in which the virus was very promptly carried by the blood current from the lungs to the distant organs. It is probable that the plague bacilli first entered the lungs by inhalation, multiplied in the alveoli, and invaded some of the interalveolar capillaries, where they formed solid thrombotic masses. Particles of the latter taken up by the blood current reached the kidneys, liver, spleen, etc., where in several instances they grew into completely obliterating emboli. It is a most remarkable fact that, in spite of the many bacterial foci interpolated into the vascular system, the general blood current did not become flooded with bacteria. In general the lumina of the vessels, both large and small, are found free from bacteria. Another point of great practical importance may be learned from a histologic study of this case, namely, that not merely the sputum but vomited matter, feces, and urine may be highly infectious.

## GROUP VI. PRIMARY PLAGUE SEPTICÆMIA.

### CASE No. 20. PRIMARY PLAGUE SEPTICÆMIA.

[Necropsy Protocol No. 983. L. T. T., Chinese, male, 28 years of age, from No. 211 Santo Cristo Street, San Nicolas. Sick for ten days; died June 4, 1904, at 1 a. m. Post-mortem examination made fifteen hours after death.]

The body of a rather small, slender, young male Chinese, about 25 to 30 years old. Nutrition only fair, rather emaciated. The

skin is somewhat cyanotic. There are no ulcerations, wounds, or recent scars. Rigor mortis is absent; the post-mortem lividity is well marked. None of the external lymphatics are palpable. On section of the body a considerable amount of very dark, fluid blood escapes. The serosa of the stomach and intestines is very much congested and the small vessels stand out very prominently. The serous membranes are rather dull. A few hemorrhagic spots are seen in the peritoneal covering of the stomach and of the small intestines. The serous covering of the bladder likewise shows a few petechiæ. The abdominal fluid is somewhat increased, slightly turbid, and rather dark yellowish. The pleural sacs contain a normal amount of amber-yellow turbid fluid. Firm adhesions are found in the region of the apex of the right lung. The pericardium shows many engorged vessels, but is otherwise normal; so is the pericardial fluid in amount, color, etc. Heart: The left ventricle is well contracted, while the right one is dilated. The external surface shows several dozen irregularly distributed subepicardial hemorrhages, varying in size from a small punctiform dot to an area of 0.5 to 0.6 centimeter in diameter. The myocardium is of fair consistency and light pink with a little tinge of yellow. No further dissection of the heart is made, since it is to be photographed. The large vessels are normal. The lungs are expanded and heavy and the external surface is more or less deep bluish-purple. This color is most intense over the lower lobes, on which also a few ecchymotic spots are seen. On section the pulmonary tissue is brown in color and full of blood. In the left lower lobe there is some admixture with grayish-yellow, but there are no areas of distinct consolidation. A good deal of blood and serous fluid can be pressed out of the pulmonary tissue. The mucous membrane of the bronchi, the trachea, and the larynx is swollen and highly injected. The base of the tongue is much swollen and cedematous. The bronchial glands are quite dark, but not materially, if at all, increased, in size, or markedly softened. The spleen is enlarged to about twice its normal size; the capsule is wrinkled and grayish-bluish-purple in color. On section the organ is dark reddish-brown. The pulp is very soft and protrudes over the surface, which is quite granular. The trabeculæ and Malpighian bodies are distinct. Kidneys: The capsules are smooth and transparent and grayish-bluish-purple in color; they peel off easily. The external surface shows a few small subcapsular hemor-

rhagic spots. On section the glomeruli and straight vessels are much engorged, the uriniferous tubules grayish-yellow and the surface dull. The mucosa of the pelves is injected, showing a very few small punctiform hemorrhages; the ureters likewise exhibit a few petechiæ. The mucosa of the bladder is thickened and contains very numerous, densely crowded small petechiæ. The suprarenals are swollen, soft, and yellowish-brown in color. The liver is large, with rounded margins. Its capsule is smooth and transparent and externally is bluish-purple, alternating with yellowish-gray. On section the surface is dull and grayish-yellow and the veins contain much blood. The consistency is markedly increased; the acini enlarged. The gall bladder is distended with a good deal of dark green viscid bile. The ducts are open; there are no stones. The mucosa of the stomach and the small intestine shows numerous small, irregular hemorrhagic areas. Both the superficial and the deep lymph glands are very little, if at all, enlarged, though they are markedly congested, particularly the mesenteric and the inguinal ones.

*Anatomical diagnosis.*—Congestion and œdema of the lungs; fatty degeneration of the liver; acute parenchymatous nephritis; multiple subserous and submucous hemorrhages (lungs, heart, kidneys, ureters, bladder, stomach, intestines). Plague septicæmia.

Smears from the different organs, including the glands, spleen, liver, lungs, etc., show a moderate number of plague bacilli. Tubes inoculated from the blood, the lungs, and the glands developed typical plague bacilli, but the cultures were contaminated by a small diplococcus.

*Microscopic examination.*—The histologic changes in the kidneys are very profound. There is universal cloudy swelling and fatty degeneration of the tubular epithelium. The tubules are generally filled with a granular detritus, and in many instances sharply outlined hyaline casts are found. These hyaline masses are composed of a homogeneous material (staining with eosin and somewhat with methylene blue): however, this does not give the tinctorial fibrin reaction. While the degenerative changes of the renal epithelium are most pronounced in the convoluted tubules, they are also present in the straight ones. The glomerular capillaries are generally not much altered, but here and there a partial hyaline (fibrin) thrombosis can be seen. Occasionally one observes an inter-tubular thrombosed vessel. Plague bacilli are found in small

groups in some of the glomeruli; they are also observed both in the capillaries and between them. A very few isolated organisms are encountered in the interstitial connective tissue between the tubules. The liver parenchyma cells show fine and coarse vacuolation. Interlobular inflammatory foci composed of small mononuclear cells are seen here and there, but the interlobular fibrous connective tissue is not increased. The interlobular capillaries and the vessels in general are much engorged with numerous, densely crowded red blood corpuscles. In a number of places inside the capillaries groups of plague bacilli are seen. However, this infection of the hepatic blood system is not general, the bacilli being confined to a number of more or less isolated spots. A good deal of granular bile pigment is found scattered throughout the hepatic tissue. The pulmonary sections show greatly engorged capillaries and veins, with an increased number of leucocytes in some of the latter. In a number of places the capillaries contain groups of plague bacilli. The alveoli contain desquamated epithelia and here and there a little extravasated blood. Otherwise there are no grave changes. No plague bacilli are seen in the alveoli. Spleen: The follicles are hazy in outline, the boundaries of the pulp spaces are indistinct and the latter are densely crowded with red blood corpuscles. The cells forming the follicles contain many large mononuclears with a large hyaline protoplasmic body. A considerable number of nuclei in the large hyaline mononuclears show a general pyknosis or lumping of the chromatin into dense granular masses. Plague bacilli generally are disseminated in moderate numbers throughout the splenic tissue, and in some parts of the pulp in larger groups. A very few of the smallest vessels contain hyaline fibrin thrombi. The inguinal lymph glands show much dilated and engorged vessels and an increase in the connective tissue at the hilum. Plague bacilli are seen here and there in little isolated groups. In the gastric mucosa the hemorrhagic spots are situated directly below the surface. The extravasation has taken place from the interglandular capillaries. These hemorrhagic areas are found to contain fairly numerous plague bacilli. It is perhaps possible that the portal of entrance of the plague bacillus in this case was the lungs. However, since no areas of consolidation were found and the infection of the lungs was quite moderate, the case has been classified as one of primary plague septicæmia.



# ANALYSIS OF THE TWENTY CASES REPORTED AND SUMMARY OF PATHOLOGICAL FINDINGS.

An analysis of the twenty cases of plague reported above shows that the total figure is made up of:

	Cases.
Group I. Primary uncomplicated bubonic plague.....	11
II. Primary bubonic plague with secondary plague septicopyemia.....	4
III. Primary bubonic plague with secondary plague pneumonia..	1
IV. Primary uncomplicated plague pneumonia.....	2
V. Primary pneumonia with secondary septicopyemia.....	1
VI. Primary plague septicaemia.....	1

Sixteen of these twenty cases were of the bubonic type, three of the pneumonic, and one of the septic type. Of the bubonic cases there were:

	Cases.
Inguinal buboes .....	11
Axillary buboes .....	1
Cervical buboes .....	4

The great preponderance of the bubonic type of plague cases is fully in accord with the observations made by the Indian Plague Commission on a very large amount of material; and the preponderance of inguinal buboes over cervical and axillary ones is likewise the rule among races and in localities where the people in general are barefooted. Of the cases of cervical buboes there were three found in children, among whom their occurrence is the most common, and one in a man of 63. Twelve of the 20 cases occurred in native Filipinos and 8 in Chinese, 15 in males, and 5 in females. The great preponderance of males over females is partly due to the fact that in one part of the affected population—namely, the Chinese—the greater proportion consists of males. However, even in India the number of cases in males greatly exceeds that in females, though not in the proportion of three to one. As to age, the cases reported range from 5 to 63 years, which is in accord with the general experience gained on a large scale. The majority of our twenty cases—viz. thirteen—occurred between the ages of 20 and 40. Almost all of the plague victims came from the lowest walks of life of the native and Chinese population. One of the cases was that of a Chinese shopkeeper or merchant.

### PORTAL OF ENTRANCE OF THE VIRUS.

As is well known, the portal of entrance of the plague virus can not always be found. In the sixteen bubonic cases there were seven in which even the slightest indication of the probable portal of entrance was absent (cases Nos. 1, 5, 6, 7, 8, 12, and 14). In the majority of the remaining nine cases of bubonic plague proper the portal of entrance was more or less unmistakably indicated. But in connection with this subject one must not forget that a secondary skin plague lesion might be mistaken for the primary portal of entrance. This is of course particularly liable to happen in cases in which but little, if anything, is known of the clinical history. Where a reliable clinical history can be obtained such a mistake is less liable to occur. In the three pneumonic cases, the portal of entrance of the virus was the lungs, because the changes in the bronchial glands were such as to destroy the probability of their being the first focus of infection. In case No. 20—primary plague septicæmia—there was no evidence of an intestinal origin; however, one might in this case suppose that the bacilli were inhaled, without causing a distinct pneumonia, entering the blood current almost immediately and in this manner producing a general septicæmia without any manifest focal localization.

### PERIOD OF INCUBATION.

The period of incubation of plague, as a rule, is a short one. The Indian Plague Commission has compiled a table of cases in which the time of infection could be fixed beyond doubt, it being contracted during post-mortem examinations or during some similar manipulation of fatal human plague cases. From their table it appears that the period of incubation generally ranges from one to five days.

"While thus," the report of the Commission (Vol. V, p. 88) says, "no facts have been reported to us which establish that the incubation period may be prolonged beyond the period of five days, the limit fixed by the numerous cases detailed above, \* \* \* we think that it is a matter of importance to point out, that where the plague first takes the form of *pestis minor*, and where afterwards *pestis minor* develops, owing to some subsequent loss of resisting power, into typical bubonic plague, there is a possibility of a considerable interval elapsing between the time at which the infection was contracted and the time at which the clinical symptoms became typical. Such cases, important as they are in the epidemiological study of the disease, as indicating one of the possible

but quite exceptional ways in which plague may be carried about to distant centers over sea, are, it must be observed, of extremely rare occurrence. One such case has, however, come unofficially to our knowledge in Poona."

#### THE LYMPH GLANDS IN BUBONIC PLAGUE.

In the majority of cases the portal of entrance of the plague bacillus is through the skin or the mucous membranes. We have already emphasized the fact that there is no case of human plague on record in which the entrance of the bacillus through the intestinal mucosa could be demonstrated beyond doubt. After the plague bacillus has gained access to the body, it generally travels through the lymph channels to the nearest gland or glands, where it then multiplies. Indeed, the multiplication of this organism in the lymph glands in most cases of bubonic plague is undoubtedly in excess of any other bacterial proliferation in any other infection, not excluding lepra. In the lymph glands the changes produced may vary from comparatively minor ones to those of the most profound degree. From a study of the lymph glands in the various stages of the infection it appears that the first change produced is vascular dilatation and engorgement and œdematous infiltration with a perivascular proliferation of the connective tissue elements. Even in cases of mild infection, one generally finds an increase of connective tissue at the hilum and usually marked vascular dilatation and œdema of the gland. The effect of the toxins and the other metabolic products of the proliferating bacilli clearly brings about an early damage to the vessel walls. However, this damage may not find a pronounced morphologic expression. From statements made in literature it appears that a well-marked hyaline degeneration of the vessel walls is always found. We can not confirm this observation, because we have frequently found an infected gland with vessels, the walls of which, to all intents and purposes, appeared to be morphologically intact. However, there always is noticeable a great dilatation and engorgement of the vessels, factors which, as we well know from general pathology, are perfectly sufficient so to damage the vessel walls as to render them pervious to the serum and to the corpuscular elements of the circulating blood. Hence, it is not necessary, in order to explain some of the tissue changes in plague, always to look for a degeneration of the vessel walls with grave morphologic changes. After a

condition of dilatation and engorgement of the vessels with general œdema of the gland tissues has been established, diapedesis of the red blood corpuscles occurs; so that, as a rule, a lymph gland infected to any extent with plague bacilli shows blood extravasation. When the infection has become very extensive and the number of bacilli very great, we generally encounter the most profound tissue changes in the glands, associated with extensive blood extravasation. To the naked eye a gland in this condition appears much swollen, more or less softened, and from dark scarlet to brownish-red, with yellow or yellowish-red mottling. Since the blood extravasation extends beyond the gland proper, the periglandular tissue is likewise of a hemorrhagic color. The tissues in the neighborhood of the gland are œdematous to a considerable extent. If the finer histologic changes of the gland are studied, it is found that the original tissue has frequently become necrotic; the differentiation into cortical and medullary portions and into follicles and cords is lost. The capsule of the gland has become loosened by œdematous and cellular infiltration, and the latter extends far into the periglandular tissue. Most of the original cells of the gland show evidences of nuclear disturbances (pyknosis, etc.) and of coagulation necrosis, and a large number of red blood corpuscles infiltrate the entire tissue and invade the periglandular areas. The vessels are greatly dilated and engorged and their walls are frequently loosened by hydropic swelling and cellular infiltration; or they may be in a condition of more or less complete hyaline degeneration. Not infrequently one finds proliferated lymphatic endothelia in larger numbers in the infected glands; these endothelia may or may not show phagocytic properties, other cells or plague bacilli frequently being included in them. Plague bacilli are often present in the glands in dense zooglœal masses. From such a center of enormous infection the bacilli infiltrate the rest of the gland and the periglandular connective tissue in more or less continuous groups. In several of our cases we have seen in extensively infected and hemorrhagic glands, a perfectly homogeneous vacuolated hyaline material, which has a strong affinity for eosin and which we consider a derivative of degenerating, agglutinated red blood corpuscles. In fact, sometimes the derivation of the hyaline material from this source becomes so obvious that there can be no doubt of its origin.

## FIBRIN FORMATION IN THE GLANDS AND IN THE OTHER ORGANS.

The homogeneous material just described is not true fibrin, and does not give the tinctorial fibrin reaction of Weigert. However, in plague true fibrin is found in the primary bubo in quite a number of cases as well as in the organs distant from the focus of infection. We encounter perfectly solid hyaline fibrin thrombi, or some vessels may be partly occluded by a hollow tubular wall thrombus or by a more or less open reticulum of fibrin. Such reticula, particularly in the bubonic glands and in the spleen, are also found in an extravascular location. Occasionally one sees threads connecting the intravascular and extravascular fibrin reticula. Sometimes fibrin is found, not in the shape of threads, but as granular, more or less solid material, always of course giving a typical Weigert's reaction. In the glandular buboes we observed fibrin in the shape of hyaline, vascular thrombi, or in the form of extravascular fibrin reticula, with or without a connection of the intravascular and extravascular deposits (in seven cases, Nos. 2, 9, 10, 11, 12, 15, and 20). Further fibrin formation was observed in the spleen in five cases (Nos. 5, 10, 11, 12, and 20), and in the lungs in three (Nos. 17, 18 and 19). Fibrin may be found in several organs in the same case (No. 10, in the primary bubo, the spleen, and the kidneys); or it may be found in the primary bubo and nowhere else (Nos. 1, 3, 7, and 17); or it may be encountered in the organs distant from the primary bubo without being present in the latter (Nos. 11, 12, and 15). In cases Nos. 18, 19, and 20, types of primary pneumonia and primary septicæmia, there were of course no lymphatic buboes present and no fibrin was observed in any of the lymph glands. Fibrin thrombi in the kidneys were found in seven cases. (See below "Hyaline Fibrin Thrombi of the Glomerular Capillaries.")

## HEMORRHAGES INTO THE BUBO AND INTO THE DISTANT ORGANS.

In studying the histopathology of the infected lymph glands we encounter other changes besides fibrin formation. These changes are quite characteristic for plague and are found not only in the glands but in locations distant from the focus of infection.

The feature which is most characteristic of plague infection is its tendency to produce a general dilatation and engorgement of

the vessels and subserous, submucous, parenchymatous, and interstitial hemorrhages. The most common locations of the latter are the epicardium, the pleura, the peritoneal covering of the stomach and intestines, and the mucosa of the stomach and intestines. There may also be subcapsular renal hemorrhages and blood extravasation into the pelves of the kidneys, the ureters, the bladder, and the male and female genital organs.

In bubonic plague proper hemorrhages into the buboes are very rarely absent. In only two of our sixteen cases of bubonic plague proper were they not present; in these death was clearly due not solely to the pest infection, but to a complication of circumstances (Case No. 8, Banti's disease; Case No. 16, ambulatory plague, terminating by embolism of the pulmonary artery). In fourteen out of sixteen cases the primary bubo showed a hemorrhagic condition. The heart in most of our cases showed subserous hemorrhages. In this organ they were found seventeen times, varying in size from a few small petechiæ to numerous and not infrequently large ecchymotic spots. The other internal organs, arranged in the order in which hemorrhages occurred in them most frequently are as follows: Stomach, fourteen times; intestines, eight; kidneys, six; bladder, three; and liver and ureters, each twice. Other organs in which hemorrhages were occasionally found are the gall bladder, the epiglottis, the esophagus, and the thymus. The most extensive and most widespread hemorrhages were found in Case No. 12—namely, one of bubonic plague in a male Filipino with secondary septicopyemia and metastatic dissemination of the bacilli. The primary inguinal bubo itself showed most extensive hemorrhages and an uninterrupted continuation of them from Scarpa's triangle up to the right kidney, involving in the area of blood extravasation all the glands, the periglandular tissue, the sheaths of the large vessels, and the perirenal, loose areolar tissue. The heart, the kidneys, the ureters, the bladder, the liver, the stomach, the œsophagus, and the small and large intestines, all showed either subserous or submucous hemorrhages, or a combination of both; blood extravasation was also seen in the anterior mediastinum. On the other hand, Case No. 8, one of the primary inguinal uncomplicated bubonic type, did not show a single hemorrhage. This is the case in which we found a spleen weighing 865 grams and a cirrhotic liver. It is reasonable to suppose that this patient had no resistance to the

plague infection and succumbed speedily before the characteristic tendency to free hemorrhage could become manifest.

The Austrian commission, in particular, held that multiple hemorrhages in plague are dependent upon the direct presence of bacilli. However, this view is not adopted by most observers; agreeing with the majority of authors we are strongly opposed to it. In all of our cases we examined the hemorrhagic areas carefully and in the larger number of them found the petachiae and ecchymoses free from them. Plague organisms were found only exceptionally in the hemorrhagic areas, and only in such cases as showed a septico-pyemic dissemination of the bacilli. To repeat, in the greater number of cases of the uncomplicated types of bubonic plague, we were unable to detect any bacilli in the numerous subserous and submucous hemorrhages.

The German commission was never able to find any bacilli in the juice obtained from the petechiae; and several authors have reported the typical occurrence of hemorrhages in guinea pigs killed by dead cultures of plague bacilli. We have likewise succeeded in producing extensive blood extravasations in distant organs in guinea pigs killed by intraperitoneal injections of dead cultures. Hence, we must hold that the hemorrhages are entirely independent of the local invasion of living plague bacilli and are due to the toxins which have entered the general blood current.

#### PLAGUE AS A RULE NOT A GENERAL MICROBIC INFECTION.

In uncomplicated cases of bubonic plague, even when the infection of the glands is extensive, bacilli are generally not found in the vessels. In fact, one may observe an area composed almost exclusively of zoöglöeal masses of bacilli, in which there is still found a vessel with a comparatively intact wall and with a lumen entirely free from plague bacilli. In the introduction we have already called attention to the fact that the results of our investigation do not justify us in classifying plague, in the strict sense of the word, as a general hemorrhagic septicæmia, but as a local infection with general symptoms and a general hemorrhagic toxæmia.

From a histologic study of our material, we have come to the conclusion that a general dissemination of the bacilli from the glands is the exception and not the rule. Usually the infection

remains localized in a gland or in a group of glands. However, there does occur a final agonal dissemination of the organisms, which does not differ in character from that of other micro-organisms in other diseases. In a number of cases an extension of the invasion by bacterial metastatic emboli does take place, but even in these instances there is no evidence that the plague bacilli multiply throughout the entire blood system, although we encounter either more or less numerous metastatic emboli, generally in the liver and the kidneys.

#### THE INFECTION OF THE SPLEEN.

However, one organ is perhaps infected in every case of plague—the spleen. The pest bacillus, even in uncomplicated bubonic cases, always gains access to its pulp spaces, and here it evidently finds conditions favorable to its multiplication.

In this respect plague may be likened to typhoid fever, in which we also have a primary infection of the lymphatic tissue (Peyer's patches) with an infection of the spleen which is never absent. Another parallelism between typhoid fever and plague may be found in a secondary infection of the lungs. Just as we find secondary typhoid pneumonia dependent upon the presence of enormous numbers of typhoid bacilli in the lungs, so we find secondary plague pneumonia dependent upon the presence of enormous numbers of plague bacilli in these organs.

That cases of plague are usually not complicated by a general septicæmic dissemination of the bacilli is also strongly indicated by the result of blood examinations on living human beings. (For an abstract of literature on this subject see Herzog and Hare: *Does Latent Plague Exist, etc.?*)

#### EXTENSION OF THE PRIMARY BUBO.

After a gland has once become infected by plague organisms and been invaded by enormous numbers of bacilli, it is usual for the other lymphatics of the same chain to suffer likewise; the latter then present the same gross and finer pathologic changes as the former. For instances, it may happen that the first gland to be invaded is a femoral one, from which the infection spreads from gland to gland until it reaches the retroperitoneal lymphatics high up in the abdomen. As in some of our cases, we may then find a



continuous chain of glands, swollen, softened, and hemorrhagic, extending from below Pupart's ligament to the kidneys and embedded in a completely hemorrhagic and gelatinous connective tissue. The same may be true of the axillary glands where the typical changes and the hemorrhages may extend from the axillary space into the thoracic cavity, and in the case of the cervical glands, from the most superficial cervical to the deepest submental lymph nodes and even in to the mediastinal glands.

#### THE OTHER LYMPH GLANDS IN PLAGUE.

Aside from the primary bubo with its hemorrhagic glands of the first, second, third order, and so on, the glands in general may present a greatly varied appearance, and we find all gradations from the most profound to very insignificant changes. In septico-pyemic cases metastatic emboli may be carried from the primary bubo into a distant gland, and there establish a secondary bubo, which does not differ materially either macroscopically or microscopically from the former. But even in uncomplicated cases, without septico-pyemia, the distant glands may be much swollen, greatly softened, and highly congested, or they may practically show no changes at all. Only a few glands may be affected, or many of them may exhibit marked pathologic changes. In general, the rule holds good that the more marked the tendency to widespread, subserous and submucous hemorrhages, the more pronounced the swelling, etc., of the lymph glands, both superficial and deep. In plague pneumonia the bronchial glands may have the appearance of a primary bubo, or they may merely show some swelling, softening, and congestion, without any blood extravasation. The lymph vessels proper, aside from those situated in the infected glands themselves, are as a rule not much changed, excepting those which connect the different glands of the chain forming the primary bubo.

#### THE HEART AND THE CIRCULATORY SYSTEM.

As a rule the heart does not show any very pronounced changes in plague, aside from those which are found as common features in the various organs in this disease. The great frequency of subepicardial hemorrhages has already been pointed out. The coronary vessels are generally greatly dilated and engorged, and the smaller ones of both the visceral and the parietal layers of the

pericardium are often distinctly visible as red tortuous streaks and lines. The pericardial fluid is normal or somewhat turbid and occasionally more or less increased in amount. The left ventricle is contracted and the right one sometimes considerably dilated. We have never seen endocardial hemorrhages or endocarditic processes. However, Duerck has described a case of plague pneumonia with endocarditis verrucosa of the mitral valve, further complicated by a purulent leptomeningitis of the convexity. This case was evidently one of septico-pyemic plague endocarditis. The myocardium is frequently of good consistency and of normal color; although sometimes it is rather soft, flabby, friable, pinkish-yellow, and easily torn. Both sides generally contain chicken-fat clots and much dark, fluid blood. The great vessels present no changes peculiar to plague; but in Case No. 16, an ambulatory one, we found an embolism of the pulmonary artery. In general the veins and capillaries are dilated and engorged to such an extent that some of the internal organs, more particularly the lungs and the kidneys, are not only greatly congested but highly œdematous. If one considers the great dilatation and engorgement of the vascular system and the œdematous infiltration of the tissues met with in plague, one is inclined to think of a hydremia of the blood. Such a condition might easily be brought about in consequence of the vasomotor and secretory disturbances which exist in plague, namely, scanty or suppressed urine and dry skin on the one hand, with great thirst and a larger ingestion of fluid on the other. Whether a hydræmia of the blood really exists in plague is a point, which, as far as we know, has never been determined. This question could, of course, not be decided by a count of the corpuscles, but only by exact chemical methods for determining water and dry residue.

The dilatation and engorgment of the vascular system often shows the smallest veins in the serous and mucous membranes as distinct, more or less tortuous lines, while the overfilling of the capillaries in the membranes named produces a uniform deep hyperæmia. In areas of this kind petechiæ and ecchymoses are encountered. Microscopically the myocardium often does not show any marked changes. In other cases a moderate degree of fatty degeneration, pigmentary degeneration of the perinuclear zone, fragmentation or segmentation are met with. However, in general, the histologic changes of the myocardium are insignificant. We

have never been able to find any bacilli in the subepicardial hemorrhagic areas.<sup>1</sup>

### THE LUNGS.

The lungs, in uncomplicated cases of bubonic plague as well as in complicated ones, in fact in all cases of pest which we have examined, show great congestion and œdema, with a corresponding diminution of the amount of air contained in them. The external surface is generally of a deep purplish color; the cut surface discharges a large quantity of blood and serous fluid. The mucosa of the bronchi, the trachea, and the larynx is more or less swollen, congested, and reddened. Hemorrhages are found on the pleural surfaces and sometimes on the mucosa of the bronchial tract, including the larynx; in one of our cases they were found in the epiglottis. In cases of primary or secondary plague pneumonia we find interlobular foci in the lungs, varying in size from that of a mere point to that of a hazelnut. They are generally well consolidated and in color grayish-reddish-white to brownish-red. They are, as a rule, surrounded by a ring of intensely congested, deep reddish-brown pulmonary tissue. The areas of lobular consolidation may become confluent so as to produce a picture of complete lobar consolidation. We have not observed such cases, but others have established their occurrence.<sup>2</sup> In one of ours the pneumonic area reached to the pleural surface, where it had produced a localized exudative, fibrinous pleuritis. In general it is found that if the areas of lobular consolidation are situated near the surface, the pleura in this region is somewhat prominent and uneven, and is quite well differentiated from the surrounding surface. In plague pneumonia the bronchial glands may or may not assume the character of primary buboes. They may be enlarged, greatly softened, and hemorrhagic, or they may show but very

<sup>1</sup>No mention of the myocardium is generally made in the microscopic reports of the twenty individual cases reported above. However, the heart and other organs not specifically mentioned, such as the suprarenal glands, the pancreas, male and female genital organs, etc., were examined microscopically in most of the cases. Since no changes of a marked character or of particular interest were found, these findings have not been given in detail but are only referred to in the summary.

<sup>2</sup>In case No. 18, the same which showed the localized fibrinous pleurisy, most of the left lower lobe was consolidated. So this case came very near being a lobar pneumonia.

little change. On microscopic examination we find that the alveoli are either filled with larger or smaller numbers of bacilli or with a cellular exudate consisting of leucocytes, alveolar epithelia, and erythrocytes, mixed with smaller or larger numbers of plague bacilli. The interalveolar septa are generally widened by an œdematous infiltration and by a swelling of the cells and fibers. The capillaries are greatly dilated and engorged; they may be free from plague bacilli or may contain metastatic emboli in complicated cases. Fibrin may be either present or absent.

#### THE SPLEEN.

Much emphasis has been laid upon the enlargement of the spleen in plague. Some observers have even gone so far as to state that this organ is always markedly enlarged in this disease and not infrequently very much increased in bulk. However, we have, among our post-mortem material four cases (Nos. 4, 5, 10, and 17) in which the spleen was not enlarged and two (No. 14, Filipinos sixty-three years old, and No. 18, Chinese twenty-seven years old) in which it was very small. On the other hand, most cases of plague show a considerable increase in the size of this organ, which then is generally about two to three times the bulk and weight of the normal one (Cases Nos. 1, 2, 7, 9, 12, 13, 15, 16, 19, and 20). In three cases (Nos. 3, 6, and 8) a very considerable enlargement was found, in one of which at least an increase of the organ to 20 by 12 by 7 centimeters and a weight of 865 grams, was clearly due to causes existing prior to the plague infection. One must not forget that splenomegaly is a very common finding in the Tropics: and hence if a very large spleen is encountered in a plague case the possibility of this being due to some other cause must always be kept in mind. We have taken great pains to search for the Donovan-Leishman bodies in those of our plague and in other post-mortem cases which showed extensive enlargement of the spleen, but we have never encountered them. This demonstrates, to a certain extent at least, that all cases of tropical splenomegaly can not be attributed to the Donovan-Leishman infection. In plague the enlarged spleen is generally, though not always, soft in consistency, dark purplish-blue externally, and dark brownish-red on the cut surface. On section the pulp generally protrudes and a large quantity of juice can usually be scraped off. The trabeculæ as a rule are distinct, but the follicles are commonly not very clear.

Why the latter are not readily distinguishable is easily explained by the microscopic examination of the organ, which frequently shows small follicles indistinct in outline, owing to the fact that the cells forming them are lost in the surrounding pulp spaces. The latter themselves are generally not distinct and are occluded by cellular elements, consisting of red blood corpuscles and nucleated leucocytes. In a considerable number of our cases the spleen gave evidence of an extensive proliferation of the endothelial cells of the pulp spaces. Sometimes great numbers of these are seen, many of them containing two or more nuclei. A number of them are phagocytic and include either other cells or plague bacilli. As already stated, in all of our cases the spleen showed an invasion with bacilli, so that we are much inclined to look upon this as a regular occurrence in plague.

#### THE GENITO-URINARY SYSTEM.

It had already been emphasized by Virchow that in plague the genito-urinary system often presents subserous and submucous hemorrhages. This is the common observation of all who have studied the pathology of the disease, and it is also confirmed by our work. As a whole the kidneys invariably show marked congestion, and even to the naked eye evidences of parenchymatous degeneration are never absent. On the cut surface there are seen uriniferous tubules which are greyish-white or grayish-yellow as well as dull, and engorged vessels, among which are the glomerular capillaries. The Malpighian tufts are usually observed as intensely red points, although at times they may appear as more or less solid, grayish-red masses. This latter appearance may easily be overlooked until our attention has been drawn to it by a microscopic examination, which fully explains why one might expect to see such solid, grayish-red, swollen glomeruli.

A microscopic change which has been described by all who have studied the kidney in plague is profound cloudy swelling of the epithelium of the uriniferous tubules, with the presence of granular or hyaline material in the latter.

#### HYALINE FIBRIN THROMBI OF THE GLOMERULAR CAPILLARIES.

However, a very characteristic change in the kidneys which we have found in seven of our twenty cases, has not, it appears, before been described, namely, a hyaline fibrin thrombosis of the glomeruli.

lar capillaries. These capillaries may be entirely or partly occluded by genuine fibrin thrombi, which give Weigert's staining reaction. The thrombi are either solid or hollow tubular wall thrombi. Where they are found, it can generally be shown that they extend into the afferent and efferent vessels and beyond these into the intertubular ones. A careful study of the vessels fails to show any appreciable morphologic change of their walls. The vascular endothelium generally appears intact; occasionally some of the lining endothelium may be missing, but this is certainly not general, but rather exceptional. The fibrin thrombi are evidently formed independently of the presence of plague bacilli in the kidneys; because in most of the cases where we did encounter them in our material a very careful search for these organisms in sections failed to reveal them. However, in one case in particular there was a simultaneous occurrence of hyaline thrombi and bacillary emboli. In some places the bacilli were actually located between the vessel wall and the thrombus. However, since this was seen only in one case, it is very clear that it was merely a coincidence; a causal nexus between the bacilli and the thrombi did not exist. The very characteristic hyaline fibrin thrombosis of the glomerular capillaries does not appear to be found frequently in acute infectious diseases in which the kidneys are greatly involved, nor, in fact, in any form of acute or chronic nephritis.

Welch, however, appears to consider it as not at all an uncommon occurrence, and makes the following statement in regard to it: "Capillary hyaline thromboses are common in the lungs in pneumonia, and in hemorrhagic infarcts. In general infective and toxic states they may be present in the liver, the lungs, and *above all, in the kidneys*.<sup>1</sup> The most striking example of this form of thrombosis with which I am acquainted is encountered in renal capillaries, chiefly of the glomeruli of swine dead of hog cholera; or of animals infected with the hog cholera bacillus. In extreme cases there is complete anuria, and it may be impossible to force more than a minimal amount of injecting fluid into the renal vessels. Section stained with Weigert's fibrin stain look as if the capillaries had been injected with Berlin blue. Ribbert found similar hyaline thrombi in the kidneys of rabbits inoculated with *S. Pyogenes aureus*. I have repeatedly found them in various experimental infections and in human infections. They occur in eclampsia. Bacteria are not necessarily present, so that toxins are probably the underlying causative factor, and for this there is experimental evidence."

It must be borne in mind that the term "hyaline thrombosis of the

<sup>1</sup> Italics our own; not in the original.

glomerular capillaries" is frequently very loosely used by authors who have written on changes of the kidneys in infections and it generally refers to an ordinary hyaline degeneration and not to a true hyaline thrombosis. In fact, a very careful study of the literature impresses one with the conviction that the latter is very rare. It has been mentioned with some emphasis in connection with only one renal affection, namely, late post-scarlatinal nephritis. Our attention was first called by Klebs to the changes in the glomeruli in diseases of the kidneys who introduced the term glomerulo-nephritis and who stimulated further research into this histo-pathologic change. He states that after scarlatina, the kidneys are found either slightly or not at all enlarged and very rich in blood, and the glomeruli appear as small, whitish points, which in sections are seen to contain little blood and are darker and more cloudy than the uriniferous tubules. However, neither Klebs nor Langhans, who studied kidneys with glomerular lesions in twelve cases of scarlatina, say anything about hyaline fibrin thrombi in the glomerular capillaries. The latter states expressly that the fibrin cylinders in the tubules are composed of a hyaline material which is not identical with fibrin. Boehm, Goemans, Fichera, and Scafiddi<sup>1</sup> have recently published contributions to the pathologic histology of the glomerulus, but they have not seen any fibrin thrombosis of the glomerular vessels. The last two authors describe hyaline degenerations of the glomerular capillaries and state that in the kidneys, with changes in the glomeruli in the kidneys, there frequently occur affections of the capillaries. The process begins in some loops, which become glass like and transparent and take certain stains homogeneously. The process then spreads to several which become fused and so form a homogeneous mass poor in nuclei. The few nuclei left show profound disturbances, such as karyolysis or karyorrhexis. In still more advanced cases one sees, in place of the glomerulus, a body smaller than the smallest glomerulus, which is globular and bounded by a capsular membrane. The body itself consists of a homogeneous, transparent, uniformly stained, hyaline mass, which shows no capillaries at all or only traces of them, and in which no more capsular space can be recognized. Nuclei, if present at all, are either small or poorly stained, shrunken, pyknotic, or fragmented. The cause of the necrosis and hyaline degeneration of the glomerular capillaries may probably be attributed in this case, as in others to profound disturbances of nutrition of the vessel walls and to obliteration of the capillaries which prevents the blood circulation. Fichera and Scafiddi expressly mention that the process described is different from true capillary thrombosis as it has been observed in post-scarlatinal nephritis. Pearce investigated the histopathology of the kidney in twenty-three cases of scarlatina, but did not find glomerular thrombosis in any of them. Hansemann microscopically examined the kidneys in 120 cases with special reference to the changes found in the

<sup>1</sup> Fichera and Scafiddi's quite exhaustive study contains a complete list of the literature and quotes 110 articles on the normal and pathologic histology of the glomerulus.

Malpighian bodies. His material included the following diseases: Nephritis, after cold, parturition, scarlatina, diphtheria, measles, croup, pneumonia, typhoid, erysipelas, puerperal fever, endocarditis ulcerosa, malaria maligna, constitutional syphilis, tuberculosis, eclampsia, atrophia infantum, encephalitis neonatorum, cholera nostras, epidemic meningitis, empyema without tuberculosis, carcinoma, pernicious anemia, leukemia, sunstroke, and chlorate of potash-phosphorus-lead and arsenic poisoning. In none of these affections did he ever find a hyaline fibrin thrombosis of the glomerular vessels; in fact, he does not mention it, though he speaks of amyloid degeneration. Posner is probably the first writer specifically to mention the presence of typical fibrin in the kidneys, however, not in the glomeruli but in the interior of the tube casts, found in the kidneys of rabbits after the ligation of the renal artery. Israel observed reticula of fibrin in the convoluted tubules, and solid fibrin masses in the capsular space of the glomeruli in experimental anemic necrosis induced by ligation of the renal artery. He evidently did not see fibrin thrombi in the glomerular capillaries, because no mention is made of such an occurrence. Engel reports the observation of five cases of chronic nephritis accompanied by glomerulitis with the presence of fibrin threads in the capsular space. These threads gave a positive Weigert's staining reaction. Nothing, however, is said about the presence of fibrin in the glomerular capillaries, Kahlden describes a case of post-scarlatinal nephritis with complete anuria, in which he observed an obliteration of the glomerular capillaries by a fibrillar and granular material which he considered to be typical fibrin. The glomerular fibrin thrombi were continued into the vasa afferentia and efferentia and frequently beyond these into the arteriola recta. However, Kahlden was not successful in staining the thrombi satisfactorily by Weigert's method, as his tissues had all been fixed in Flemming and in Mueller's fluids. Friedlaender, according to the preceding writer, previously described a type of post-scarlatinal glomerulo-nephritis which manifests itself from three to four weeks after scarlatina and which is characterized by oedema, albuminuria, oliguria, or even anuria. The microscopic examination of the kidneys in such cases shows glomerular capillaries changed into solid, sausage-like masses, making it scarcely possible to differentiate the wall of the capillary from its contents. Whether Friedlaender looked upon this thrombotic material as fibrin does not appear. Ernst found fibrin in the capsular space of the glomeruli and also in the interior of the hyaline tube casts in cases of nephritis. No mention is made of fibrin thrombi in the glomerular vessels. Ribbert, speaking of glomerulo-nephritis in one place and hyaline thrombosis in another, mentions hyaline fibrin thrombi as occurring occasionally in the glomerular capillaries. Tschistowitsch, one of the most recent writers on obliteration and hyaline degeneration of the glomeruli, does not mention hyaline fibrin thrombosis.

From a review of the literature on the subject of glomerular changes in nephritis it would certainly appear that hyaline fibrin thrombosis of the glomerular capillaries is a rather rare occur-



rence, which has been more fully described only in connection with late post-scarlatinal nephritis and with swine plague by Welch. It would probably be a thankless task here to attempt an explanation of the formation of hyaline fibrin thrombi in the vessels of the kidneys and of other organs, particularly in the infected lymph glands in plague. Indeed, such an attempt at explanation would open up the whole question of blood coagulation and of fibrin formation inside and outside the blood vessels. Loeb has quite recently published an experimental contribution to this subject. With reference to thrombosis and the formation of fibrinous exudates he expresses the view that after the removal of the vascular endothelium the specific substances causing coagulation are extracted from the tissues. The ferments acting upon fibrinogen, held in colloidal solution, precipitate it in the form of fibrin. However, in most of our renal sections, in which hyaline fibrin thrombosis has been seen in the glomerular vessels, the vascular epithelium was to all intents and purposes morphologically intact and well preserved. It is of course not at all unreasonable to suppose that the plague toxins acting as they appear to do in particular upon the kidneys, so damage the vascular epithelium that it becomes pervious to the coagulating ferments, before any morphologic changes indicate a serious functional disturbance.

#### THE URINE IN PLAGUE.

That the kidneys are profoundly affected in plague is illustrated not merely by the findings on the post-mortem table and by microscopic examination of the sections but by the clinical history of the disease.

The German commission reports that it found albumen in the urine in most cases of plague in which a urine examination was made, while hyaline and granular casts and few or numerous blood corpuscles were seen occasionally. Calmette and Salembini state that it is only in grave cases that the urine is diminished or entirely suppressed. They sometimes saw bloody urine, and always found it very acid and with traces of albumen. Aoyama states that the albuminuria is generally moderate. Bitter found albumen in most cases, generally very moderate in amount; but in fatal cases it was invariably present. Yamagiwa found albumen only rarely. The Austrian commission examined the urine in forty-five cases and found albumen present in all of those where repeated examinations were made. The most extensive urine examinations in plague have been made by Cathorn in India. She found albumen absent in only 24, or 7 per cent. out of 341 fatal cases; while in 256 nonfatal cases it was

absent in 64, or 25 per cent of them. In some of our cases, with a septicopyemic dissemination of the virus, we have found an extensive infection of the kidneys with plague bacilli; and the conclusion is justified that the bacilli must be abundant in the urine in such cases. In fact in articles on plague one frequently finds the statement that the urine generally contains bacilli; yet exact observations on this point have thus far been very meager.

The German commission reports that it found plague bacilli in the urine in only two cases. The urine both from plague patients and from post-mortem cases usually was found free from these organisms. The Austrian commission frequently found numerous plague bacilli in the kidneys, but encountered them in only five out of seventeen different specimens of urine obtained post-mortem from plague cases. The Indian commission examined sixty specimens of urine by cultural methods and found the plague bacilli three times. Five other specimens were examined by inoculation into guinea pigs; in one case only did an animal develop plague.

These results obtained from the bacteriologic examination of urine in plague are well in accord with our own histologic observations. The bacilli were as a rule found in the renal tissue only in moderate numbers and in such situations that their appearance in the urine was not at all likely. Only when found in the capsular space of the glomeruli may we safely suppose them to have been present in the urine also. However, since one can not know *inter vitam* whether an infection of the kidneys exists or not, it is well always to treat the urine in plague as a possible source of infection. The same rule applies to feces, which likewise, as the histologic study of the stomach and intestines teaches, may sometimes contain plague bacilli.

However we may here insert that the presence of plague bacilli in the feces must be still more exceptional than their appearance in urine.

The German commission was never able to demonstrate them in the feces either by culture or by animal inoculation. The Indian commission, after giving a detailed account of its work on the attempted detection of plague bacilli in the feces, says: "The results of the above series of examinations may be summarized in the statement that the plague bacillus as yet has not in any case been isolated from human feces. Such a negative result is, however, of very little account in view of the fact that it is, as we have seen, a matter of extreme difficulty to isolate by cultural methods the plague bacillus from a material such as feces, in which the bacillus coli and an infinity of other bacteria are to be found."

The pelves of the kidneys, in intensely hemorrhagic cases, occasionally contain a considerable amount of blood. In such cases the

bladder may likewise contain bloody urine or even blood coagula. Like the mucosa of the pelves, that of the ureters and the bladder occasionally shows petechiæ and ecchymoses.

The suprarenals are generally somewhat swollen, enlarged, softened, and congested, and darker in color than normal. We have not found any marked histologic changes in them, aside from dilatation and engorgement of the capillaries, conditions which are particularly noticeable in the interfascicular capillaries of the cortex.

#### THE LIVER AND THE GALL BLADDER.

The liver is generally of normal size, though it may be slightly enlarged. In those cases where we have found a decrease it was clearly not due to the plague infection but to morbid conditions previously existing. The capsule is smooth and tense; its external color is deep purplish-blue or purplish-pink. Evidences of a minor or more pronounced degree of fatty degeneration are rarely missing. Alternating with the general purplish color we find areas which are grayish-white or grayish-yellow. The cut surface shows a brownish-red or ocher-yellow color according to the degree of fatty infiltration and degeneration, and the veins discharge much blood. In septicopyemic cases we encountered necrotic, soft, grayish-white foci. These may also shine through the surface and may have been noticed before the organ is cut into. The liver lobules are either distinct or more or less indistinct; and their boundaries may frequently be even more distinct than under normal conditions, which is due to the fact that interacinous, periportal, inflammatory foci are often encountered in the liver in cases of plague. They were found in cases Nos. 1, 2, 3, 7, 8, 9, 10, 14, 16, 17, and 20. The microscopic examination, aside from these foci, further shows dilated, engorged capillaries. The parenchyma cells are finely or coarsely vacuolated or in a condition of cloudy swelling or more or less complete granular degeneration. In uncomplicated cases of bubonic plague the parenchyma cells are not profoundly changed; but in septicopyemic cases the change is generally quite profound. The necrotic foci, if present, contain large numbers of bacilli and frequently show capillaries more or less completely occluded by metastatic emboli. The cells in this neighborhood are in a condition of complete coagulation necrosis, which extends beyond the groups of bacilli into the adjacent tissues. Phagocytic, proliferated endothelia are sometimes seen in the liver.

The gall bladder is generally normal; but it may sometimes be profoundly changed, showing numerous subserous hemorrhages and a completely œdematous and almost gelatinous condition of the wall. The bile itself varies from a normal consistency and golden-yellow color to a pitchy condition and almost black color. The serosa of the gall bladder, like that of the liver, occasionally shows extensive ecchymotic spots.

We have not encountered any marked macroscopic or microscopic changes in the pancreas.

### THE STOMACH AND THE INTESTINES.

The stomach and the intestines are generally markedly affected in plague. Petechiæ and ecchymoses are found both in the serosa and in the mucosa. Particularly the gastric mucosa is generally in a hemorrhagic condition. The petechiæ often extend into the duodenum and occasionally even into the esophagus. Microscopically, the mucosa of the stomach always shows greatly dilated interglandular vessels and frequently hemorrhages between the glands and into the uppermost layers of the mucosa or even upon its free surface. Plague bacilli were found in these areas only in septicopyemic cases. The upper layers of the mucosa are often necrotic; and the cells of the peptic glands, even where the membrane is still fairly intact, show evidence of nutritive disturbance (multinuclear cells). The small and large intestine in general frequently show a great congestion of the mucosa and serosa with petechiæ and ecchymoses. In one case submucous blood cysts were found in the large intestine; these were probably due to the plague infection, as other, higher parasites could not be demonstrated in them. In a considerable proportion of our material the intestinal follicles were more or less swollen, viz, moderately in cases Nos. 6, 7, 15, and 17, and markedly in cases Nos. 1, 5, and 12, and highly in case No. 2. In the other cases the intestinal lymph follicles were normal.

### STEPS IN ESTABLISHING THE POST-MORTEM DIAGNOSIS OF PLAGUE.

We shall now mention briefly, but systematically, all observations and experiments which will in a given case of suspected fatal plague enable us to come to a definite and conclusive diagnosis. However, it must be borne in mind that there are some exceptional

cases in which a diagnosis is impossible. When a plague infection has run its course without having in itself killed the patient, he may nevertheless succumb to a secondary pyogenic complication, to parenchymatous degeneration of the internal organs or to exhaustion due to toxemia, any one of which may carry off the victim after the plague bacilli have disappeared from the primary bubo and from the system at large. Of course such exceptional cases are of no great epidemiological importance, since a spread of plague can not occur if no more bacilli are present. In the great majority of fatal cases of human plague the post-mortem diagnosis, to one familiar with the disease and with the ordinary technique of bacteriological investigation offers no particular difficulties. The diagnosis of plague in rat cadavers which are much decomposed is a matter of much greater difficulty, but in this article this is a subject with which we not concerned.

The report of the Indian Plague Commission (Vol. V, p. 442) gives the following description of the body of a patient dead of plague:

The body, if undisturbed, is stated to be generally lying on one side, with the knees flexed, and the head slightly bent on the chest. The skin in dry, and in a few cases petechiæ and purpuric spots may be seen; the muscles are soft, as the rigidity of death is delayed; the features retain a fixed, anxious appearance; the eyes are half closed and sunken, with the pupils dilated; and the tongue is swollen, and although it sometimes has the appearance displayed during life, not unusually it is covered with a dry, almost horny dark or yellowish-brown and cracked fur. In pneumonic cases, the body seems especially shrunk and collapsed and has a livid aspect, and blood-stained sputum is often found adherent to the lips. Our attention was drawn by Captain Elphink, I. M. S., to the existence of œdema, extending over the front and sides of the chest, the abdomen, and the upper part of the arms, which had been observed by him and by Captain Chaytor-White, I. M. S., in all plague corpses, and was believed to occur immediately before death. If this condition is generally present, it would be valuable as an aid in determining if death had been caused by plague, and especially in cases where no buboes are present. It has not, however, been observed by the great majority of those who in India have had the opportunity of seeing large numbers of fatal cases, both before and after death.

This guide to the post-mortem diagnosis of plague is evidently not intended for the pathologist performing a necropsy, but for the general practitioner or the layman-sanitary inspector of India. But we seriously doubt whether anybody will be materially assisted in a plague diagnosis by so vague a description as that given

above. The general œdema which is mentioned we have never seen in any of our plague cases.

The following are the steps in a systematic plague necropsy:

(1) *External inspection of the body*.—As the most characteristic points brought out by the external inspection of a body dead of plague we would mention the following: The bubo is generally present in the femoral, the axillary, or the cervical region, and consists of a rather firm, doughy swelling over which the skin is generally adherent while the surrounding tissue is markedly œdematous. In the neighborhood of the bubo may be seen an ulcer or a carbuncle with extensive necrosis. As a whole the surface of the body is frequently cyanotic; skin eruptions, petechiæ, and ecchymoses are commonly observed. A dark, blood-tinged, foamy, serous fluid always oozes from the nostrils of a plague body when it is turned over. This is due to the great congestion and œdema of the lungs, which we have never failed to observe in any of our cases.

(2) *The dissection of the body* shows the multiple, interstitial subserous and submucous hemorrhages, the general congestion of the organs, the spleen tumor, the parenchymatous degeneration of the kidneys, and the lobular consolidation in pneumonic cases, described in detail above.

(3) During the post-mortem examination inoculations of agar and salt-agar tubes or plates and gelatin plates are to be made from the bubo, or as the case may be, from the consolidated areas of the lungs, the spleen, the heart's blood, and other organs, particularly if they show areas of focal necrosis.

(4) *Preparations of smears* from the same locations are to be made on slides, which as soon as air dry are immersed in absolute alcohol.

(5) *Pieces of tissue* from the primary focus (lymph glands or lungs), from the spleen, and from the necrotic foci, are to be collected and placed in sterile, empty test tubes or Petri dishes.

(6) *Pieces of tissue* are to be fixed in Zenker's solution for the subsequent histologic examination.

(7) *Animal inoculations*.—After the termination of the autopsy the pieces of tissue preserved in sterile receptacles are to be used for inoculation into guinea pigs. A number of these animals are infected by the cutaneous method (Gohn and Albrecht) by rubbing some of the juice from the bubo (or lung) and the spleen on the

shaved abdomen. Other animals should receive subcutaneous and intraperitoneal inoculations of the suspected material triturated with sterile physiologic salt solution.

(8) *After twenty-four hours* the tube and plate cultures are to be examined with the naked eye, with the aid of the magnifying glass and in stained cover-glass preparations. The animals likewise are to be examined. Some of those which have received intraperitoneal injections are liable to succumb to the plague infection after twenty-four hours.

Martini has worked out a special method in the examination of guinea pigs infected cutaneously. Since this method often enables us to make a definite diagnosis in doubtful plague cases after forty-eight hours, it is to be recommended. His method is as follows:

(a) The material suspected of containing the plague bacilli is triturated with about three times the quantum of sterile bouillon. This emulsion is rubbed with the back of a knife on the shaved abdomen of several (five or six) guinea pigs.

(b) After twenty-four hours the guinea pigs are examined for swollen lymph glands, and if any are found, their juice is drawn with a sterile syringe and inoculated into agar tubes, and also examined in smears.

(c) If what appear to be plague bacilli are found in the smears, two rats are inoculated intraperitoneally with the juice obtained from the enlarged gland of the guinea pigs.

(d) The cultures obtained from the juice are examined macroscopically and microscopically and tested with an antiplague serum of known agglutinating power.

The agglutination test can not be made, it should here be stated expressly, with antiplague sera selected "at random," because some have little or no agglutinating power, as has been repeatedly pointed out by several observers, including the Indian Plague Commission. (Vol. V, p. 68 of report.)

Kolle and Martini recommend the desiccated antiplague serum of the Pasteur Institute for the agglutination test. The dry fine powder is first dissolved in ten times its weight of sterile distilled water (1 gram to 10 cubic centimeters. The solution is complete after several hours, whereupon the further dilutions necessary for the tests can be prepared. It is found that this dry serum will agglutinate genuine plague cultures, and only those, in dilutions of from 1:1,000 to 1:6,000. The less virulent the plague culture the greater the agglutinating powder of the dry serum; and vice versa, the more virulent the cultures, the lesser the agglutinating power.

Zlatogoroff, who studied the question as to how long plague bacilli remain alive and virulent in cadavers under various conditions of temperature and moisture, maintains that the cutaneous method of Gohn and Albrecht for infecting guinea pigs, is absolutely reliable only as long as the organs do not contain any considerable number of putrefactive and

other microbes. For diagnostic purposes in the case of old cadavers he therefore recommends a pernasal inoculation, which he practiced in the following manner: The lower part of one of the nasal cavities of a guinea pig is slightly wounded with a pair of sharp forceps or a needle, however, in such a manner that very little blood is drawn. A small piece, preferably of the spleen, is then grasped in fine forceps and introduced into the side where the slight trauma has been produced, after which it is well rubbed into the nasal mucosa by rotatory motions of the forceps. This method is certainly somewhat objectionable on account of the danger of inducing a fit of sneezing in the animal operated upon, with uncontrollable dissemination of the plague material. Zlatogoroff himself considers this energetic procedure a "misstand," as he expresses it, but he confesses that it is indispensable, as otherwise the test may be negative in the presence of virulent plague bacilli. It also appears that this author has not ruled out the possibility of producing by his method in guinea pigs a disease which might simulate plague, a fallacy which, according to all the testimony obtained in this matter, is impossible by the cutaneous method. Zlatogoroff's investigation, at any rate, was not made with material derived from human cadavers, but with pieces of organs from the decomposed bodies of animals infected experimentally with plague. Since his publication has appeared after our report was practically finished, we have not taken an opportunity to try his method, and hence can not recommend it.

We do not wish to create the impression that all the cultural and inoculation experiments detailed above are necessary to arrive at a reliable diagnosis of plague in each suspected case. On the contrary, one familiar with plague can generally make a diagnosis after the termination of the necropsy, as soon as the smears from the organs have been examined microscopically. But in obscure cases all of the steps mentioned above may be necessary, and **none** of them should be omitted when a first-suspected case is to be diagnosed in a plague-free locality where an incontestable diagnosis is a necessity in justifying the protective and restrictive measures which should be instituted in order to prevent the spread of an infectious disease which at times many assume such destructive pandemic proportions.



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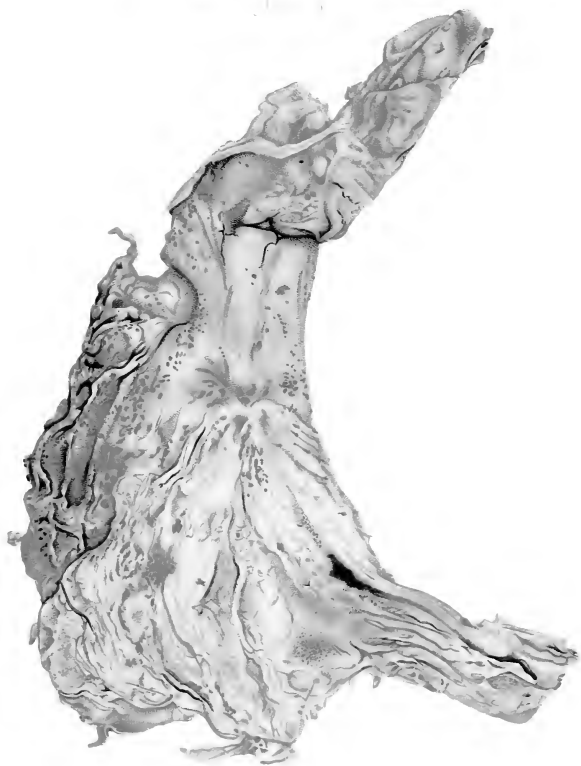
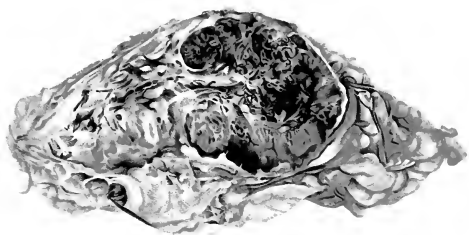
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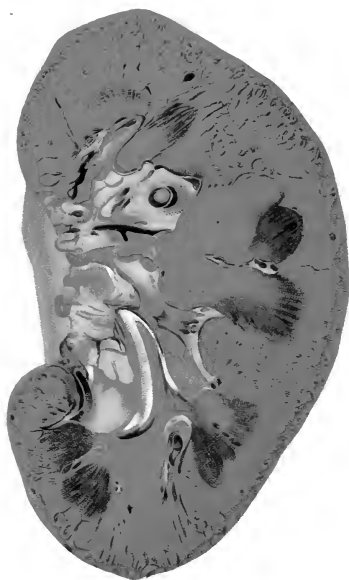










FIG. 6.

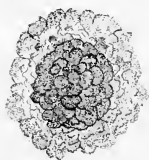


FIG. 7.

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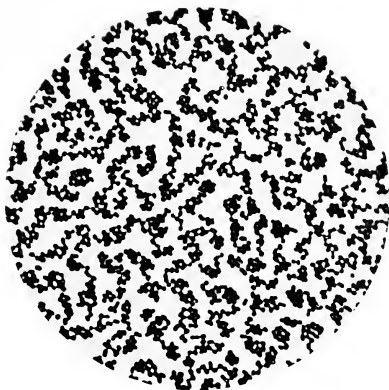


FIG. 8.



FIG. 9.





FIG. 10.



FIG. 11.

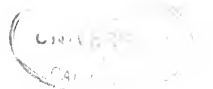




FIG. 12.

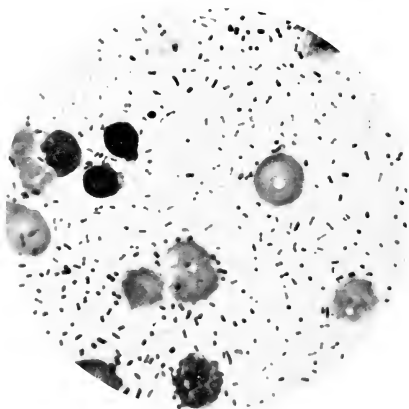


FIG. 13.



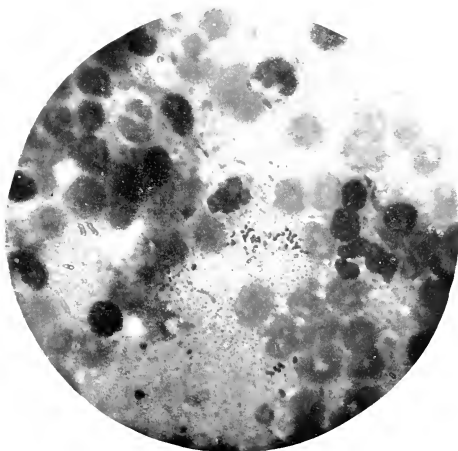


FIG. 14.

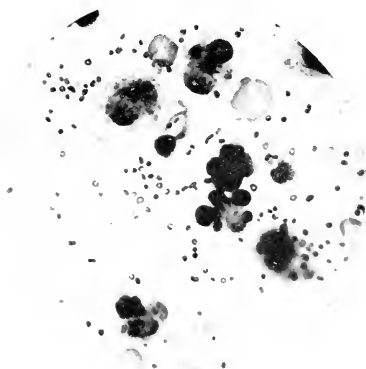


FIG. 15.







FIG. 16.

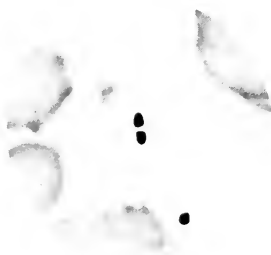


FIG. 17.



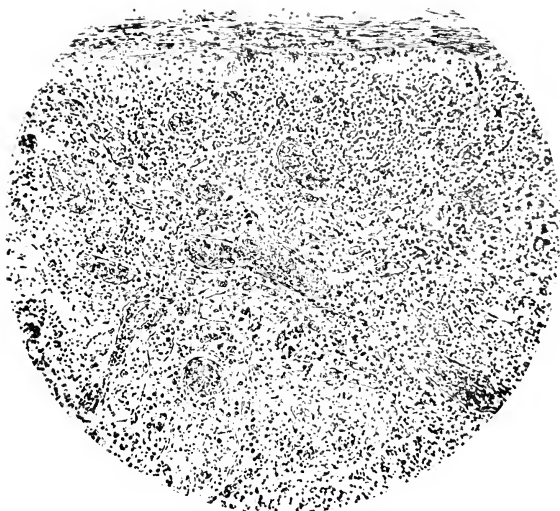


FIG. 18.

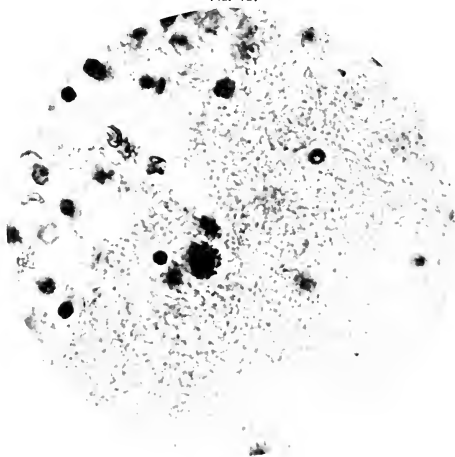


FIG. 19.



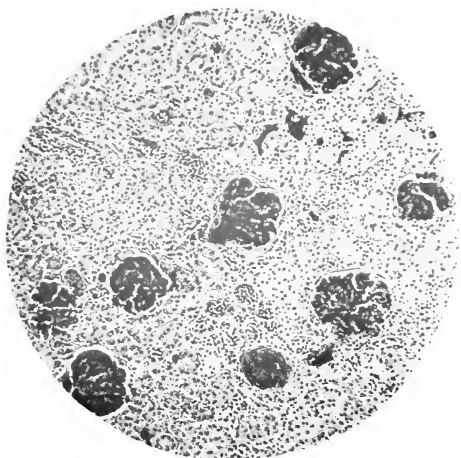
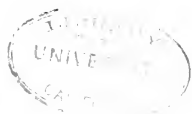


FIG. 20.



FIG. 21.



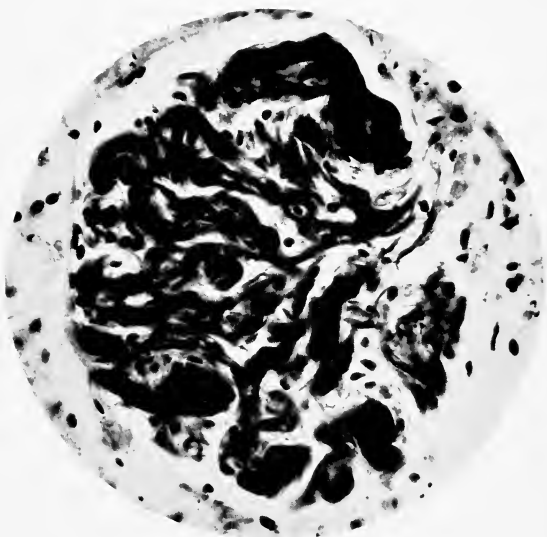


FIG. 22.







FIG. 23.



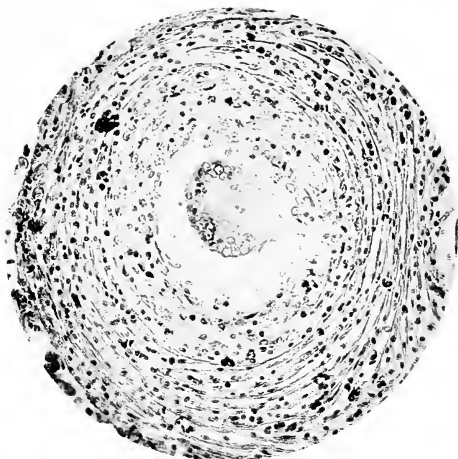


FIG. 24.



FIG. 25.





FIG. 26.

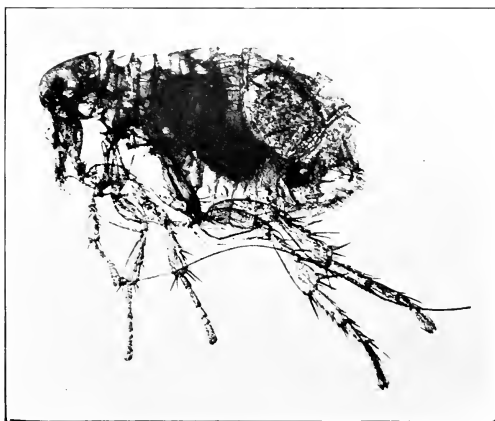


FIG. 27.





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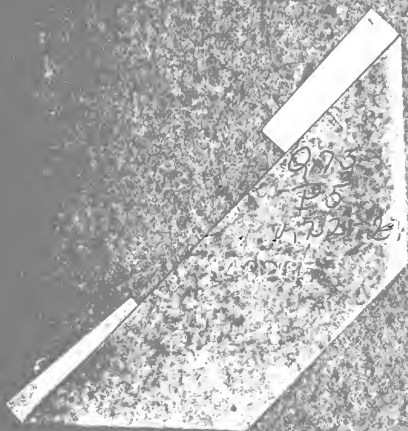
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